

Tommy Liljefors

BARRIERS TO INTERNAL
ROTATION IN SOME
DIMETHYLAMINO SUBSTITUTED
AZOLES

Experimental studies
and molecular orbital calculations

Lund 1973

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Tommy Liljefors, fil. kand., Mlm



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CONTENTS

I.	INTRODUCTION	7
II.	SYNTHESIS	12
III.	BARRIERS TO INTERNAL ROTATION	23
	III.1 Theory and method	23
	III.2 Results of the barrier determinations	28
	III.3 Discussion of the barriers	38
IV.	MOLECULAR ORBITAL CALCULATIONS	46
	IV.1 π -Electron model. The PPP approximation	46
	IV.2 All-valence-electron model. The CNDO/2 approximation	52
	IV.3 Geometries used in the calculations	54
	IV.4 General considerations in comparisons between experimental and calculated barriers	64
	IV.5 Results of the PPP calculations	65
	IV.6 Results of the CNDO/2 calculations	77
V.	CHEMICAL SHIFTS	102
VI.	ULTRAVIOLET SPECTRA	112
VII.	PREPARATIVE PART	120
	REFERENCES	130



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I. INTRODUCTION

The interaction between an amino or substituted amino group and a conjugated or aromatic system is qualitatively described as the formation of a partial double bond between the amino nitrogen atom and the atom to which the amino group is bonded:



The degree to which the amino nitrogen "lone pair" of electrons is delocalized is determined by the properties of the attached system and may be modified by changes in this latter system, for instance by different substituents. This thesis deals with the quantitative aspect of this interaction as it shows up in the barrier to internal rotation around the partial double bond and the effects of the interaction on chemical shifts and ultraviolet spectra of some N,N-dimethylamino substituted five-membered heterocycles. The compounds studied in this work are shown separately on the page following immediately after this introduction. Throughout the work, the experimental observations have been extensively compared with results obtained from molecular orbital calculations.

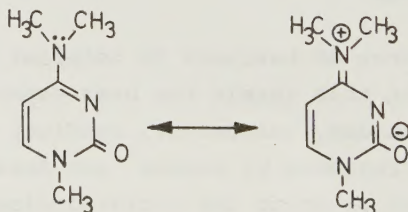
Rotational barriers

The existence of barriers to internal rotation of the type considered in this thesis has been experimentally demonstrated in amides, thioamides, amidines and similar classes of compounds, as reviewed by Binsch¹ and Kessler². Less attention has been given to the corresponding barriers in aromatic amino compounds. MacKenzie and MacNicol³ have estimated the free energy of activation $\Delta G_{133}^{\ddagger}$ (at 133 K) for the barrier to internal rotation of the dimethylamino group in N,N-dimethyl-

aniline to be 5.1 (± 1.0) kcal/mol. Substitution in the para position of the benzene ring with an electron-withdrawing substituent raises the barrier. The para-nitroso compound was shown to have a barrier ($\Delta G_{133}^\ddagger$) of 8.6 kcal/mol. These barriers are considerably lower than those found for instance in amides and thioamides, which are generally greater than 15 kcal/mol. A few papers have been published in which heteroaromatic compounds are considered. Katritzky and Tiddy⁴ have measured the barriers to dimethylamino group rotation in 4-dimethylamino-pyrimidine and nitro substituted 2-dimethylamino-pyridine and found barriers ($\Delta G_{298}^\ddagger$) of 10-12.3 kcal/mol. 2-Dimethylamino-pyridine without further substituents has a barrier of 7.6 kcal/mol⁵ ($\Delta G_{153}^\ddagger$). In spite of the facts that the barriers for these heterocyclic compounds have been measured in different solvents and the $\Delta G^\ddagger$'s are given at different temperatures, it is safe to conclude that aza substitution in the N,N-dimethylaniline and 2-dimethylamino-pyridine rings raises the barriers significantly.

Almog, Meyer and Shanan-Atidi⁶ have studied rotational barriers in some 4-dialkylaminopyrimidines, -quinazolines and -pyrido[3,2-d]pyrimidines and found free energies of activation (at the coalescence temperature) for the rotation of the dialkylamino group in the range 12.1-17.2 kcal/mol. (For some compounds steric hindrance in the initial state of the rotation process lowered the barrier.)

Relatively high barriers have also been found in some compounds of biological importance. For 1,7,7-trimethylcytosine:



a barrier to rotation of the dimethylamino group of 14.8 kcal/mol ($\Delta G_{298}^\ddagger$) has been reported⁷. The high barrier in this compound

can be attributed to the amide character shown by the resonance structures above. Dimethylamino derivatives of adenosine⁸, adenine⁹ and cytidine⁸ have C-N rotational barriers of 13.4 ($\Delta G^\ddagger_{273}$), 15.3 ($\Delta G^\ddagger_{303}$) and 15.5 kcal/mol ($\Delta G^\ddagger_{303}$) respectively.

The aim of the present investigation is to extend the studies of CN rotational barriers to five-membered heterocyclic compounds. The investigation is concentrated on the dependence of the barrier on the type of heterocyclic ring system and the influence of substituents on the barrier.

Molecular orbital calculations

The compounds studied in this thesis are, with a few exceptions, free from steric hindrance of the dimethylamino group rotation. The barrier to internal rotation should, therefore, reflect the energy of bonding interaction between the dimethylamino group and the heterocyclic ring system. It is then of interest to investigate the ability of quantum chemical models to treat this interaction. Both π - and all-valence-electron models have been used.

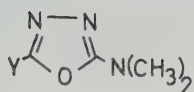
The Pariser-Parr-Pople (PPP) method which is by now the most recognized π -electron method has been used in this work, and is briefly presented in Section IV.1. Earlier attempts to calculate barriers to internal rotation by this method include compounds such as biphenyl^{10,11}, benzaldehyde¹², bithienyls¹³ and nitrobenzenes¹⁴. In most of these cases the calculations are complicated by steric interactions and/or substantial changes in core-repulsion between different conformations. The results of the π -electron calculations are, therefore, often highly dependent on the choice of potential curves which are superimposed on the PPP method. In view of these complications, it is believed that calculations of the sterically unhindered rotational barriers in the compounds studied in this work provide a more direct test of the ability of the π -electron model to account for barriers to internal rotation.

The recent development of fast computers has made it possible to use all-valence-electron models in calculations of different properties of quite large molecules. Calculations of rotational barriers, using various all-valence-electron models have for instance been performed on formamide (CNDO/2)¹⁵, benzaldehyde (CNDO/2)¹⁶, and pyrimidines (PCILO)⁶. In some calculations the results are promising for the further development of methods including all valence electrons, while other calculations have been less successful. There is evidently a need for more confrontations between theoretical and experimental results to evaluate the strong points as well as the limitations of the methods. The CNDO/2 method, which has been used in this work, is presented in Section IV.2.

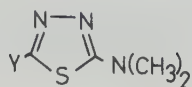
Chemical shifts and ultraviolet spectra

The delocalization of the amino nitrogen "lone pair" and the dependence of the delocalization on the presence of other substituents can be expected to determine the NMR and ultraviolet spectra of the compounds under consideration. A correlation between chemical shifts of the dimethylamino protons and Hammett σ^- -constants in para-substituted N,N-dimethylanilines has been demonstrated¹⁷, and it has also been shown that the UV spectra of these compounds are markedly dependent on the nature of the para-substituent^{18,19}. These aspects will be studied in Chapters V and VI and the experimental results will be discussed in the light of molecular orbital calculations.

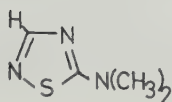
Compounds studied in the present work.



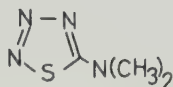
- Ia Y = NO₂ Ie Y = H
 Ib Y = CN If Y = C₆H₅
 Ic Y = CO₂C₂H₅ Ig Y = CH₃
 Id Y = CF₃



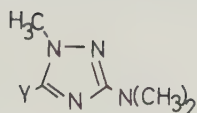
- IIa Y = NO₂ IIe Y = H
 IIb Y = CN IIf Y = C₆H₅
 IIc Y = CO₂C₂H₅ IIg Y = CH₃
 IId Y = CF₃



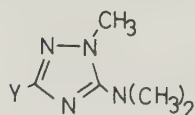
III



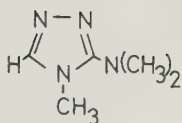
IV



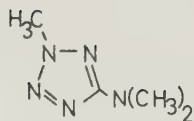
- Va Y = H
 Vb Y = CH₃



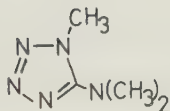
- Vc Y = H
 Vd Y = NO₂



Ve



VIa



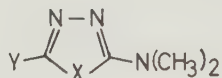
VIb

II. SYNTHESIS

2-Dimethylamino-1,3,4-oxa- and -thiadiazoles

2-Amino-1,3,4-oxa- and -thiadiazoles have been known for many years. As early as the end of the nineteenth century Pulvermacher²⁰ and Freund²¹ synthesized 2-amino-1,3,4-thiadiazoles. 2-Amino-1,3,4-oxadiazoles have been known since around 1930 from the work of Stolle and Fehrenbach²² and De²³. Earlier synthetic work on these types of heterocyclic amines have mostly been concerned with the 2-amino compounds. The 2-alkylamino and especially the 2-dialkylamino compounds have hitherto received much less attention. Thus, very few dialkylamino compounds in the 1,3,4-oxa- and -thiadiazole series have been described in the literature.

In this work the following 2-dimethylamino-1,3,4-oxa- and -thiadiazoles have been prepared:



I. X = O; II. X = S

Ia, IIa Y = NO₂

Ie, IIe Y = H

Ib, IIb Y = CN

If, IIb Y = C₆H₅

Ic, IIc Y = CO₂C₂H₅

Ig, IIg Y = CH₃

Id, IId Y = CF₃

These compounds have in most cases been prepared by methods developed for the preparation of 2-amino-1,3,4-oxa- and -thiadiazoles.

Three methods have been used:

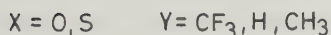
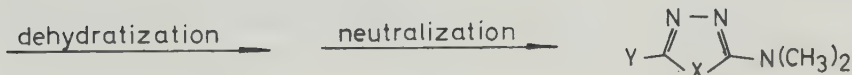
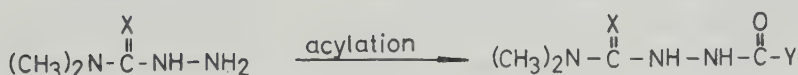
Method 1. Cyclization of an 1-acylsemicarbazide or -thiosemicarbazide by a dehydrating agent.

Method 2. Oxidative cyclization of a semicarbazone or thiosemicarbazone.

Method 3. a) Substitution on the ring.

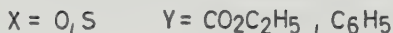
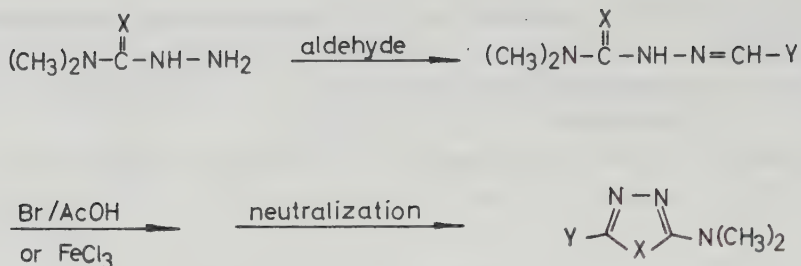
b) Reactions on the side chain.

Compounds d, e, and g in each series were prepared by method 1.



The acylations were effected by the appropriate anhydride ($\text{Y} = \text{CF}_3$ and CH_3) or formic acid ($\text{Y} = \text{H}$). In the preparations of the 1,3,4-oxadiazole compounds ($\text{X} = \text{O}$) the acylsemicarbazides were treated with phosphorous oxychloride according to Gehlen and Möckel²⁴. The acylthiosemicarbazides were cyclized by acetyl chloride in the cases where $\text{Y} = \text{H}$ or CH_3 . This method has been extensively used in preparations of 1,3,4-thiadiazoles and was first described by Pulvermacher²⁰. When $\text{Y} = \text{CH}_3$ it is not necessary to isolate the intermediate acylthiosemicarbazone, as this can conveniently be cyclized in situ, which is also the case when $\text{Y} = \text{CF}_3$. The anhydride can be used to acylate as well as to cyclize the intermediate acylthiosemicarbazone in situ.

Method 2 was used to prepare compounds c and f. The semicarbazones were oxidatively cyclized with bromine in acetic acid, a method due to Gibson²⁵. Compound If has earlier been synthesized by Najer et al.²⁶ using this method.



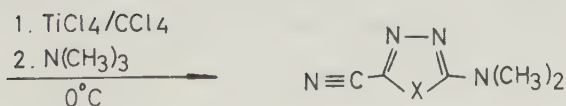
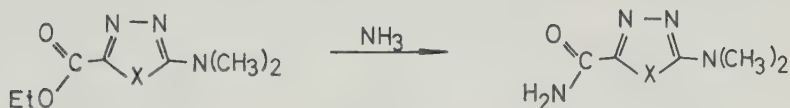
To prepare compound Ic it was necessary to isolate the hydrobromide formed in the cyclization step and then neutralize it very carefully with KHCO_3 , otherwise the yield of compound Ic becomes very low.

The thiosemicarbazones were oxidized with ferric chloride according to Young and Eyre²⁷ who oxidatively cyclized benzaldehyde thiosemicarbazone to 2-amino-5-phenyl-1,3,4-thiadiazole by this method as early as 1901. A large number of 2-amino-5-substituted-1,3,4-thiadiazoles have since been prepared by ferric chloride oxidation of thiosemicarbazones. Werber and Maggio²⁸ showed that this method could be used to cyclize thiosemicarbazones of alkyl glyoxalate to the corresponding alkyl 2-amino-1,3,4-thiadiazole-5-carboxylate. The phenylsubstituted compound IIIf has previously been prepared by Hoggarth from 1-benzoyl-4,4-dimethylthiosemicarbazide and phosphoric acid²⁹.

The nitro- and cyano substituted compounds a and b were prepared by Method 3. Electrophilic substitution on the unsubstituted 1,3,4-oxa- and -thiadiazole rings has not been recorded, and it has been reported that nitration on the unsubstituted 1,3,4-thiadiazole ring is not possible even under drastic conditions³⁰. An amino group should, however, activate the ring towards electrophilic substitution and a successful nitration of 2-amino-1,3,4-thiadiazole by fuming nitric acid has indeed been claimed in a patent³¹, but the identity of this compound

is doubtful, and the product is probably 2-nitramino-1,3,4-thiadiazole³². The 2-dimethylamino substituted compound IIe could, however, easily be nitrated by fuming nitric acid and concentrated sulphuric acid to give compound IIa in 65 % yield. The 1,3,4-oxadiazole compound Ie was also successfully nitrated by the same procedure. The oxadiazole ring is much more sensitive to the strong acid conditions required for the nitration so the reaction had to be carried out at low temperature (0-5°C) and the yield was also much inferior (27 %) than in the thiadiazole case.

The cyano substituent in compounds Ib and IIb was introduced by the following sequence:

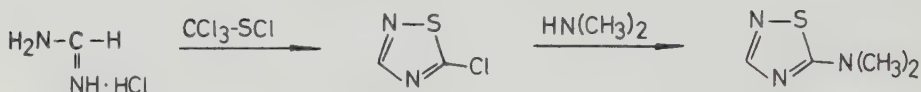


The dehydration method using titanium tetrachloride and base was developed by Lehnert³³. Attempts were first made to perform the dehydration step using refluxing phosphorous oxychloride, but this method gave only small amounts of the cyano substituted compound. Most of the starting material was recovered unchanged.

5-Dimethylamino-1,2,4-thiadiazole (III)

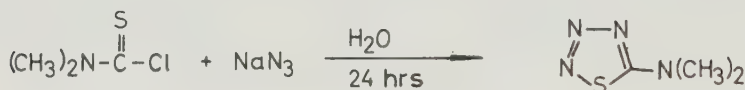
This compound was prepared from 5-chloro-1,2,4-thiadiazole and dimethylamine in ethanol as described by Goerdeler³⁴.

The chloro compound was made from formamidine hydrochloride and trichloromethanesulfenyl chloride in alkali at 0°C³⁵.



5-Dimethylamino-1,2,3,4-thiatriazole (IV)

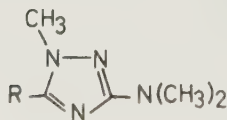
A convenient one step synthesis due to Lieber³⁶ was used to prepare this compound.



N,N-dimethylthiocarbamoyl chloride reacts with sodium azide in water at room temperature to give compound IV.

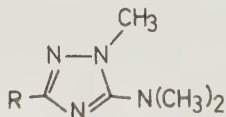
3-Dimethylamino-1,2,4-triazoles (V)

Five compounds of this class have been prepared.



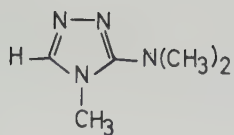
Va R=H

Vb R=CH₃



Vc R=H

Vd R=NO₂

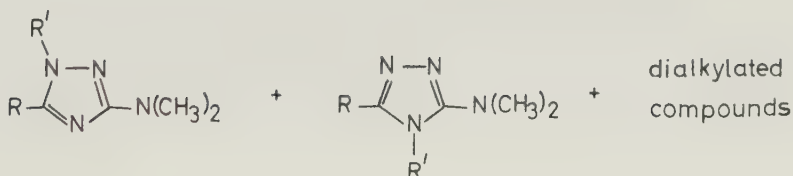


Ve

There are two main routes to obtain derivatives of 3-dimethyl-amino-1,2,4-triazoles, alkylated on ring nitrogen.

A. Alkylation of the triazole.

B. Ring closure of an appropriate acyl-aminoguanidine.

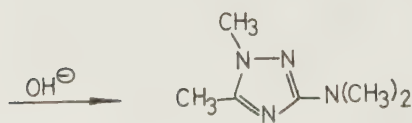
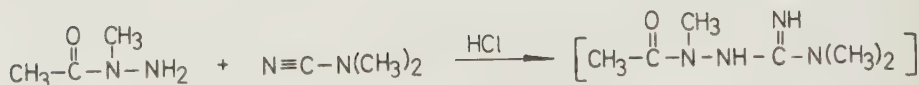




Route A usually gives a difficultly separable mixture of isomers³⁷, so no attempts were made in this direction.

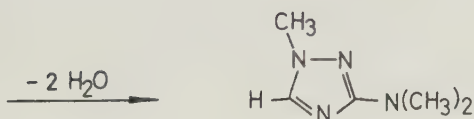
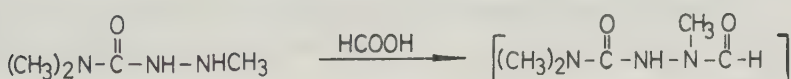
The main problem in preparing the compounds according to route B is the preparation of the aminoguanidines. It is, however, not necessary to isolate these, as they can often be cyclized in situ.

Cipens and Grinsteins^{38,39} have developed a method in which the acylaminoguanidine is formed from an acylhydrazine and a cyanamide in concentrated hydrochloric acid. The 1-acylaminoguanidine is then cyclized with alkali. Compound Vb was prepared by this method.



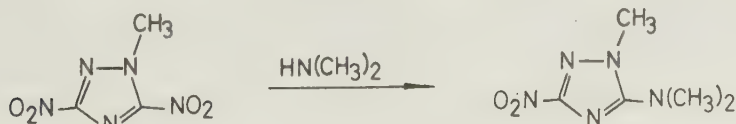
V b

When the same method was used in an attempt to prepare Va, the result was a mixture of Va and Vc. The NMR spectrum of the mixture compared with those of the pure compounds showed that Va was the major component of the mixture. Attempts to separate the mixture by distillation were unsuccessful. The formation of the isomer mixture probably depends on an isomerization of the starting material, N-formyl-N-methylhydrazine, in the reaction mixture since the purity and identity of this compound was carefully checked by NMR, gas chromatography, thin layer chromatography, and its ability to form hydrazones. The pure compound Va, as well as Vc and Ve could be prepared by heating the appropriate aminoguanidine salts with formic acid for several hours according to the method of Kröger, Schoknecht and Beyer⁴⁰. Also in this method the intermediate acylaminoguanidine is cyclized in situ.



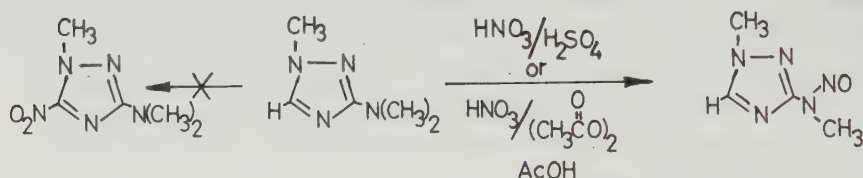
Va

The nitro derivative Vd was prepared according to Bagal, Pevzner and Samarenko from 1-methyl-3,5-dinitro-1,2,4-triazole⁴¹ by replacement of the nitro group in the 5-position by dimethylamine. By this method it is not possible to obtain the 2-methyl



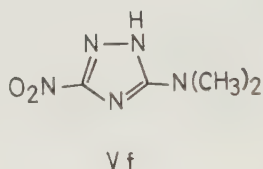
Vd

isomer only the 1-methyl compound Vd is formed. The low reactivity of the 1,2,4-triazole towards electrophilic substitution made it impossible to use ordinary nitration procedures. Attempts to nitrate compound Va in the 5-position with fuming nitric acid/conc. sulphuric acid or fuming nitric acid/acetic anhydride were unsuccessful. In both cases the N-nitroso compound was formed.

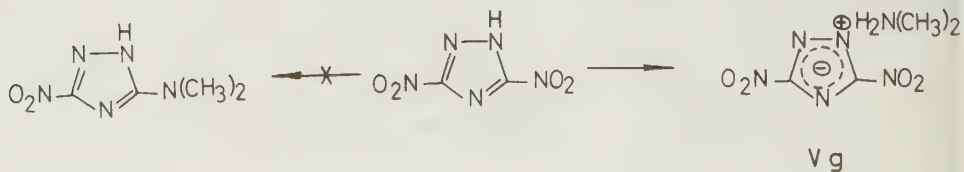


Nitroso-demethylation instead of nitration has also been observed for dimethylaminopyridines^{42a}.

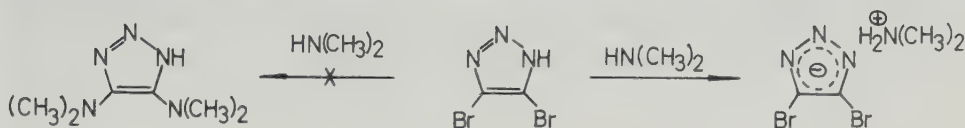
It should in principle be possible to prepare the 2-methyl isomer by methylation of Vf and separation of the resulting mixture.



An attempt to prepare Vf from 3,5-dinitro-1,2,4-triazole and dimethylamine was, however, unsuccessful.

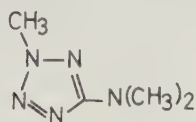


The hydrogen on the ring nitrogen proved to be too acidic and the salt Vg was formed. The salt was heated in a sealed tube with dimethylamine at 200° for 24 hrs but no further reaction took place. The formation of a salt instead of substitution has also been observed in the 1,2,3-triazole system^{42b}.

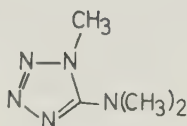


5-Dimethylaminotetrazoles (VI)

The two possible monomethylated 5-dimethylaminotetrazoles VIa and VIb were prepared.



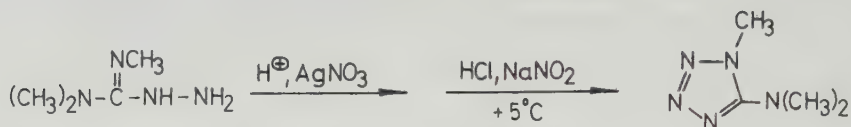
VI a



VI b

These compounds were obtained by methylation of the 5-dimethylaminotetrazole prepared according to Jensen *et al.*⁴³ Methylation with dimethyl sulphate gave an isomer mixture in poor yield in which the 1-methyl isomer (VIb) was the major product. Reaction with diazomethane, however, resulted in an isomer mixture in much better yield and this time the 2-methyl isomer (VIa) was the major product. The mixture could easily be separated by distillation. The determination of the product distributions was made from NMR spectra of the isomer mixtures in which the

position of the 1-methyl signals was known from the NMR spectrum of VIb prepared unambiguously from 1,1,2-trimethyl-3-amino-guanidinium iodide and nitrous acid⁴⁴:



III. BARRIERS TO INTERNAL ROTATION

III.1 Theory and Method

The barriers to internal rotation of interest in this work have been studied by the variable temperature NMR technique. This technique is by now well established and has been used in studies of a wide range of conformational problems. (For recent reviews see Refs. 1 and 2). The method is suitable for studies of processes with free energies of activation from 5 to 25 kcal/mol. The process considered in this work is an exchange of two groups of equivalent protons between two uncoupled sites, A and B, with equal populations, p_A and p_B . The temperature dependence of the NMR lineshape is in this case very simple. At sufficiently low temperatures, the exchange is slow and individual resonance signals from the two sites are obtained. Upon raising the temperature the signals broaden, coalesce and in the fast exchange limit the NMR spectrum consists of a single sharp line (Fig. 1).

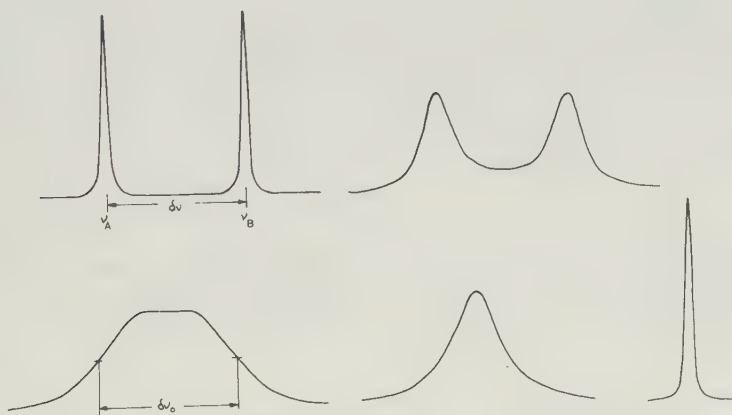


Fig. 1. Temperature dependence of the NMR spectrum.
(Two equally populated, uncoupled sites.)

The theory for exchange broadening of NMR spectra is based on the Bloch equations⁴⁵ and was developed by Gutowsky et al.⁴⁶ and McConnell⁴⁷. In the McConnell formulation the lineshape due to the exchange between two uncoupled sites A and B is described by the imaginary part of the complex magnetization G under steady state conditions, that is $\frac{dG}{dt} = 0$ (1).

$$G = G_A + G_B = -iC \frac{[\tau_A + \tau_B + \tau_A \tau_B (\alpha_A p_B + \alpha_B p_A)]}{(1 + \alpha_A \tau_A) (1 + \alpha_B \tau_B) - 1} \quad (1)$$

where τ_A and τ_B are the site lifetimes related to the rate constants through: (2)

$$A \xrightleftharpoons[k_B]{k_A} B ; \quad k_A = \frac{1}{\tau_A} ; \quad k_B = \frac{1}{\tau_B} \quad (2)$$

$$\alpha_A = \frac{1}{T_{2A}} - 2\pi i (\nu_A - \nu)$$

$$\alpha_B = \frac{1}{T_{2B}} - 2\pi i (\nu_B - \nu)$$

T_{2A} and T_{2B} are spin-spin relaxation times, and ν_A and ν_B are the chemical shifts in Hz for the protons in sites A and B. The imaginary part can be written explicitly as (3)⁴⁸.

$$\text{Im} (G) = \frac{-C\{p[1 + \tau(p_B/T_{2A} + p_A/T_{2B})] + QR\}}{P^2 + R^2} \quad (3)$$

where $\tau = p_B \tau_A = p_A \tau_B$

$$P = \tau \left[\frac{1}{T_{2A} T_{2B}} - 4\pi^2 \Delta\nu^2 + \pi^2 \delta\nu^2 \right] + \frac{P_B}{T_{2B}} + \frac{P_A}{T_{2A}}$$

$$\delta\nu = \nu_A - \nu_B; \Delta\nu = 1/2(\nu_A + \nu_B) - \nu$$

$$Q = \tau [2\pi\Delta\nu - \pi\delta\nu(P_A - P_B)]$$

$$R = 2\pi\Delta\nu [1 + \tau(1/T_{2A} + 1/T_{2B})] + \pi\delta\nu\tau(1/T_{2B} - 1/T_{2A}) + \pi\delta\nu(P_A - P_B)$$

C is an amplitude factor

The spectra were recorded at 10-14 different temperatures. The mean lifetimes τ were calculated by a computer program that minimizes the sum of the squared deviations at given frequencies between theoretical and digitized experimental spectra by the STEPIT procedure⁴⁹. Three spectra were automatically digitized at each temperature and transferred to a punched tape.

$T_2 = T_{2A} = T_{2B}$ was calculated at each temperature by formula (4)⁵⁰ used as input data.

$$T_2 = \frac{1}{\pi(W_1 + \Delta W_{\text{ref}})} \quad (4)$$

where W_1 = linewidth at half height of the NMR signal without exchange broadening.

ΔW_{ref} = the difference between the linewidth of a reference signal at the actual temperature and a temperature where no exchange broadening occurs. Tetramethylsilane (TMS) was used as reference.

The use of formula (4) rests on the assumption that the line-widths of the NMR signals studied and that of the reference signal are equally affected by changes in homogeneity and solvent viscosity.

Below the coalescence temperature $\delta\nu = \nu_A - \nu_B$ was determined at each temperature directly from the observed lineshape. At and above the coalescence temperature, $\delta\nu$ was obtained from a plot of $\delta\nu$ below coalescence versus the temperature and extrapolation to higher temperatures.

The thermodynamic parameters $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were obtained by plotting $\frac{1}{2\tau.T}$ versus $\frac{1}{T}$ according to the Eyring equation⁵¹ formulated as (5)

$$\log \frac{1}{2\tau.T} = - \frac{\Delta H^\ddagger \log e}{RT} + \frac{\Delta S^\ddagger \log e}{R} + \log \frac{\kappa k_B}{h} \quad (5)$$

where k_B = Boltzmann's constant

κ = transmission coefficient assumed to be unity

h = Planck's constant

R = gas constant

$\Delta G^\ddagger$ is obtained from (6)

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \quad (6)$$

Due to problems associated with low coalescence temperatures not all of the compounds were subjected to the total lineshape analysis described above. The barriers in these cases were studied at the coalescence temperature and the mean lifetime τ was calculated by formula (7)⁵².

$$\tau = \frac{1}{\sqrt{2}\pi\delta\nu_0} \quad (7)$$

where $\delta\nu_0$ is the linewidth at half height at the coalescence temperature.

Formula (7) is derived by differentiation of the line-shape equation for cases where $p_A = p_B = 0.5$ and $T_2 = \infty$. The formula is accurate when $\delta\nu_0$ is large compared to the linewidth at zero exchange⁴⁸, a condition which is generally fulfilled in this work.

The free energy of activation at the coalescence temperature, T_c , is in this case given by expression (8) derived from (7) and the Eyring equation.

$$\Delta G_{T_c}^{\ddagger} = 2.303 R \cdot T_c \left(\log \frac{k_B}{h} + \log \frac{T_c \cdot 2}{\pi \sqrt{2} \cdot \delta\nu_0} \right) \quad (8)$$

Temperature measurements

The temperatures were obtained from the temperature-dependent shift between the methylene and hydroxyl protons in a mixture of HCl, CD₃OH and CH₂Cl₂ sealed in a capillary and placed in the center of the sample tube. The capillary was calibrated against the Varian methanol sample, which had been calibrated against a copper-constantan thermocouple. The capillary was stored at - 20°C between measurements and was recalibrated immediately before or after each measurement, since it could be suspected that the mixture was unstable. No appreciable unstability was, however, detected during the period it was used (~ 2 years).

Instrumental

The NMR spectra were recorded using a Varian A-60 or A-60A spectrometer equipped with a Varian V-6031 variable temperature probe and a V-6040 temperature controller. Chemical shifts were measured by the side-band technique using a HP 200 CD Audio

Oscillator. The frequencies were measured with a HP 3734 A Electronic Counter. The spectra were recorded on 100 Hz sweep-width and at 500 sec. sweep time at sufficiently low radio frequency field to avoid saturation phenomena. A Univac 1108 computer was used for the calculations.

III.2 Results of the barrier determinations

Barriers to internal rotation of the dimethylamino group in compounds Ia-g, IIa-g, III and IV determined using the approximate formula (7) are summarized in Table 1. Compounds Ib, IIa, III and IV were also subjected to total lineshape analysis. The results are given in Tables 2, 3, 4, and 5 and in Fig. 2. The thermodynamic parameters obtained from Eyring plots are given in Table 6.

To make it possible to compare the barriers of the different compounds, the same solvent mixture, pyridine-d⁵/CD₂Cl₂ 2:1, was used in all of these measurements. This solvent mixture was chosen since it was able to keep all compounds in solution at sufficiently low temperatures. The limited solubility at low temperatures of especially the nitro compounds did not allow CDCl₃ or other more frequently used solvents to be used in this work. Deuterated solvents were necessary mainly to avoid overlapping of the solvent signals with the signals from the temperature capillary. The barriers in compounds Ib and IIId were also determined in pure CD₂Cl₂ to obtain an estimate of the influence of the added pyridine-d⁵ on the barriers. The approximate formula (7) was used and the results are given in Table 7. Comparing the values in this table with the corresponding values in Table 1 it is seen that the different solvent give very similar free energies of activation, $\Delta G^\ddagger_T$. The shift, $\delta\nu_o$, is, however, much smaller in CD₂Cl₂ and the T_c coalescence temperatures T_c are lower.

Comparing Tables 1 and 6 it is satisfactory to note that the $\Delta G^\ddagger_{T_c}$ values obtained from the approximate formula (7) are

Table 1. Results of barrier measurements using formula (7).
Solvent: Pyridine-d⁵/CD₂Cl₂ 2:1. (At temperatures below ~ 175 K it was sometimes necessary to add a few drops more CD₂Cl₂ to prevent the solvent from crystallizing.)

Compound	$\delta\nu_{\text{O}}$ (Hz)	T _C (K)	$\Delta G^*_{T_C}$ (kcal/mol)	ΔH^* (kcal/mol) ^c
Ia	11.0	205.2	10.6	8.4
Ib	13.4	201.7	10.3	8.1
Ic	18.2	187.6	9.4	7.4
Id	15.5	186.5	9.4	7.4
Ie		< 154	< 7.7 ^a	< 6.1
If		< 154	< 7.7 ^a	< 6.1
Ig		< 154	< 7.7 ^a	< 6.1
IIa	19.2	224.9	11.4	9.1
IIb	20.7	214.1	10.8	8.6
IIc	25.4	203.0	10.1	8.0
IId	22.2	196.2	9.8	7.8
IIe	28.8	159.0	7.8	6.2
IIIf	33.0	158.1	7.7	6.1
IIg		< 154	< 7.5 ^b	< 5.9
III	20.7	233.0	11.8	10.5
IV	16.8	248.4	12.7	10.5

^aCalculated from an assumed $\delta\nu_{\text{O}}$ value of 20.0 Hz.

^bCalculated from an assumed $\delta\nu_{\text{O}}$ value of 35.0 Hz.

^cCalculated using activation entropies from Table 6.

Table 2. Total lineshape analysis of Ib. (Solvent:
Pyridine/CD₂Cl₂ 2:1.)

T (K)	$\delta\nu$ (Hz)	T_2 (sec)	τ (sec)	$\Delta G^\ddagger$ (kcal/mol)
187.8	13.0	0.490	0.0686	10.2
192.5	12.9	0.531	0.0520	10.2
196.4	12.9	0.375	0.0324	10.2
199.4	12.6	0.289	0.0240	10.3
202.5	12.6	0.265	0.0162	10.3
204.4	12.5	0.318	0.0123	10.3
206.2	12.4	0.531	0.0107	10.4
208.1	12.3	0.531	0.0084	10.4
210.2	12.2	0.531	0.0070	10.4
212.9	12.1	0.637	0.0053	10.4

Table 3. Total lineshape analysis of IIa.

(Solvent: Pyridine-d⁵/CD₂Cl₂ 2:1).

T (K)	$\delta\nu$ (Hz)	T_2 (sec)	τ (sec)	$\Delta G^\ddagger$ (kcal/mol)
208.0	19.1	0.424	0.0817	11.3
209.9	19.2	0.424	0.0659	11.3
213.1	19.1	0.354	0.0529	11.4
216.4	19.2	0.354	0.0355	11.4
216.6	19.0	0.424	0.0364	11.4
219.1	18.9	0.398	0.0289	11.4
222.0	18.8	0.374	0.0212	11.5
224.4	18.8	0.318	0.0166	11.5
227.9	18.7	0.636	0.0116	11.5
231.4	18.6	0.578	0.0081	11.6
235.5	18.5	0.636	0.0064	11.6
239.5	18.4	0.636	0.0040	11.6
241.9	18.4	0.578	0.0032	11.7
246.7	18.2	0.636	0.0022	11.7

Table 4. Total lineshape analysis of III.
(Solvent: pyridine-d⁵/CD₂Cl₂ 2:1).

T (K)	$\delta\nu$ (Hz)	T_2 (sec)	τ (sec)	ΔG^* (kcal/mol)
212.4	21.2	0.796	0.1001	11.6
214.2	21.2	0.723	0.0857	11.7
215.5	21.3	0.796	0.0739	11.7
217.9	21.0	0.796	0.0569	11.7
219.5	20.8	0.796	0.0447	11.7
219.8	21.0	0.796	0.0411	11.6
221.9	20.8	0.723	0.0340	11.7
224.6	20.8	0.723	0.0276	11.7
228.8	20.6	0.637	0.0169	11.7
234.1	20.4	0.796	0.0089	11.7
237.3	20.2	0.723	0.0066	11.7
242.0	20.1	0.723	0.0045	11.8
243.4	20.0	0.796	0.0038	11.8
248.1	19.8	0.796	0.0026	11.8

Table 5. Total lineshape analysis of IV.
(Solvent: pyridine-d⁵/CD₂Cl₂ 2:1.)

T (K)	$\delta\nu$ (Hz)	T_2 (sec)	τ (sec)	$\Delta G^\ddagger$ (kcal/mol)
227.5	17.2	0.549	0.1249	12.6
230.9	17.3	0.692	0.0866	12.6
233.3	17.0	0.624	0.0720	12.7
238.1	17.1	0.758	0.0405	12.6
241.5	16.7	0.637	0.0308	12.7
245.8	16.7	0.637	0.0197	12.7
249.2	16.5	0.723	0.0144	12.7
253.4	16.4	0.758	0.0098	12.8
257.1	16.2	0.723	0.0075	12.8
259.8	16.1	0.723	0.0064	12.9
264.0	16.0	0.723	0.0044	12.9
268.3	15.8	0.723	0.0031	12.9

Table 6. Thermodynamic parameters from total lineshape analysis.

Compound	$\Delta H^\ddagger$ (kcal/mol)	$\Delta S^\ddagger$ (e.u.)	$\Delta G^\ddagger_{T_c}$ (kcal/mol)
Ib	8.1 $\pm$ 0.3	-10.7 $\pm$ 1.5	10.3
IIa	9.2 $\pm$ 0.1	-10.2 $\pm$ 0.6	11.5
III	10.5 $\pm$ 0.1	-5.3 $\pm$ 0.5	11.7
IV	10.5 $\pm$ 0.1	-9.0 $\pm$ 0.4	12.7

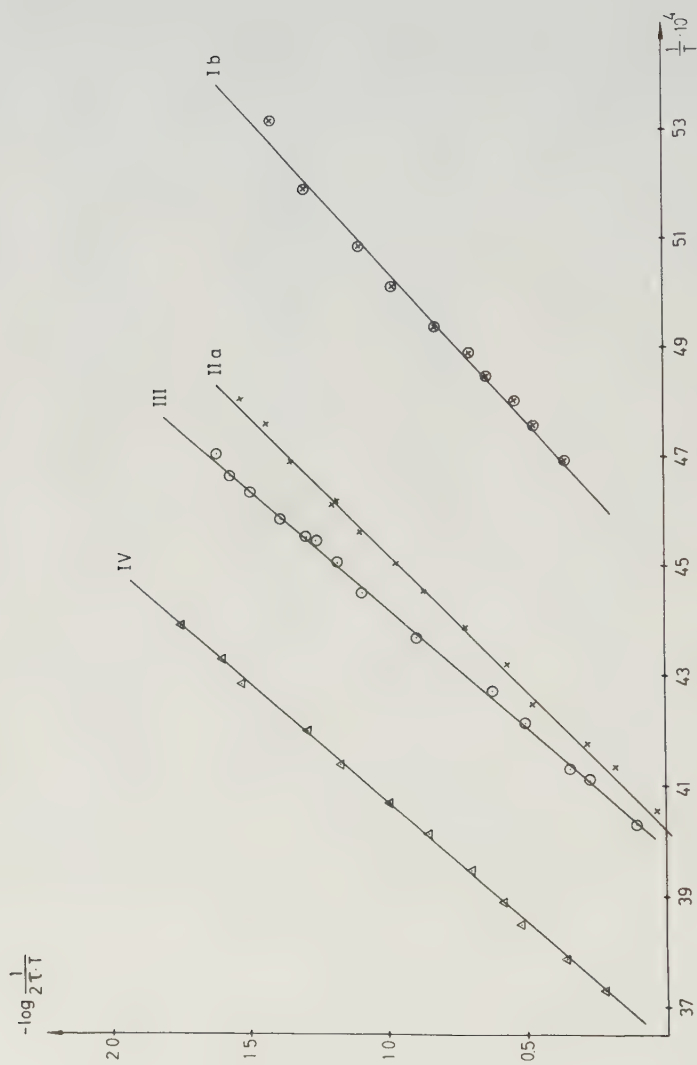


Fig. 2. Eyring plots for compounds Ib, IIa, III and IV.

Table 7. Measurements in CD_2Cl_2 .

Compound	$\delta\nu_{\text{O}}$ (Hz)	T_{C} (K)	$\Delta G^{\ddagger}_{T_{\text{C}}}$ (kcal/mol)
Ib	5.5	197.3	10.4
IId	12.4	186.8	9.5

almost identical with those obtained from total lineshape analysis. This provides experimental evidence that the assumptions on which the formula (7) rests are fulfilled for the systems in this work for which this formula has been used.

The activation enthalpies, $\Delta H^{\ddagger}$, in the last column in Table 1 were calculated from the free energies of activation at the coalescence temperature, $\Delta G^{\ddagger}_{T_{\text{C}}}$, and the activation entropies, $\Delta S^{\ddagger}$, obtained from total $^{\text{C}}$ lineshape analysis (Table 6) using formula (9). The entropies of activation are

$$\Delta G^{\ddagger}_{T_{\text{C}}} = \Delta H^{\ddagger} - T_{\text{C}}\Delta S^{\ddagger} \quad (9)$$

then assumed to be the same for all compounds in each series.

It was not possible to determine the barriers to internal rotation of the dimethylamino group in the 1,2,4-triazole and tetrazole series (V and VI). In all cases no sign of splitting or even broadening due to slow exchange of the methyl signals was observed at temperatures down to the limit of the apparatus used (ca - 120°C). The failure to observe any barriers in these systems may depend on a weak electronic interaction between the dimethylamino group and the heterocyclic ring, producing barriers too low to be measured by the present NMR technique ($\Delta G^{\ddagger} < 5\text{-}6$ kcal/mol). It may, however, also depend on the chemical shifts

of the dimethylamino methyl groups. If the shifts between the methyl groups are unobservably small, no coalescence point can of course be observed, but even if the shifts are in principle possible to observe, it follows from formula (8) that for a given value of ΔG_T^+ a smaller shift leads to a lower coalescence temperature, and the limiting factor becomes the possibility of obtaining sufficiently low temperatures. Another limiting factor in the present case is that the solvent mixture crystallizes at about -120°C .

In compounds Vc, Vd, Ve, and VIb where the ring methyl group is bonded to the nitrogen atom neighbouring the dimethylamino group, the heterocyclic ring and the dimethylamino group can probably not be coplanar for steric reasons. A twisted initial state of the rotation will increase the energy of this state relative to an unhindered planar initial state. Since the transition state should be unaffected by the methyl hindrance this will result in a decrease of the barrier. That such a decrease of a barrier can be substantial is shown by comparing the barriers of the compounds in Fig. 3. The barrier in compound (a) is 11.7 kcal/mol (ΔG_{223}^+ in $(\text{CD}_3)_2\text{CO}$), while the barrier in (b) is too low to be measured⁵³. A similar situation is found in the compounds shown in Fig. 4. The barrier in the compound shown

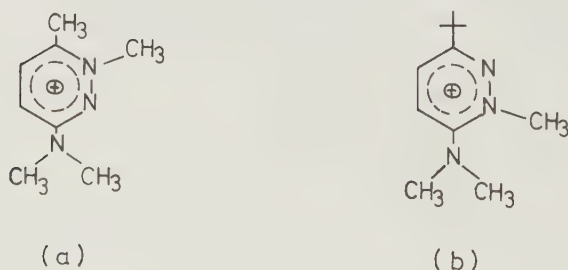
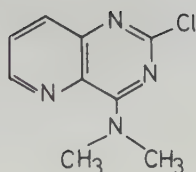
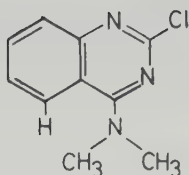


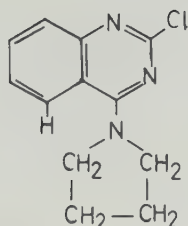
Fig. 3



(a)



(b)



(c)

Fig. 4

in Fig. 4 (a) is 13.5 kcal/mol (ΔG^*_{278} in CDCl_3), while in (b) it is < 8.3 kcal/mol $(\text{CD}_3)_2\text{CO}$ ⁶. This decrease cannot convincingly be explained by differences in resonance interaction in planar systems. It must be due to steric hindrance by the peri-hydrogen. This conclusion is supported by the increase in the barrier to ~ 12 kcal/mol when the dimethylamino group is replaced by a pyrrolidino group (Fig. 4c), which gives less steric interaction with the peri-hydrogen.

The reason for the unobserved hindered rotation in compounds Va, Vb, and VIa is less clear. Here the ring methyl is bonded to the nitrogen atom furthest away from the dimethylamino group and thus no steric interference is possible. The chemical shift between the dimethylamino methyls can, however, be expected to be small considering their similar environments, leading to low coalescence temperatures. It is thus not possible

to draw any defined conclusions about the electronic interactions in these systems relative to the other systems considered in this study.

III.3 Discussion of the barriers

1,3,4-Oxadiazoles and -thiadiazoles

The barriers to dimethylamino rotation in the 1,3,4-thiadiazole compounds IIa-d are 0.4-0.7 kcal/mol higher than the corresponding barriers in the 1,3,4-oxadiazole series (I). (Table 1). Since steric interactions are negligible in these series, this difference in barrier heights reflects a difference in bonding interaction between the dimethylamino group and the heterocyclic ring systems.

In comparisons of physical and chemical properties of oxygen- and sulphur heterocycles, the concept of valence-shell expansion on sulphur by use of 3d orbitals has often been used, as reviewed by Salmond⁵⁴. In the thiophene series, experimental evidence for contributions of the resonance structures shown in Fig. 5, which invoke valence-shell expansion, has been reported^{55,56,57}.



Fig. 5

However, there is still a great deal of controversy about the importance of such structures. (CNDO⁵⁸ and ab initio⁵⁹ molecular orbital calculations indicate that 3d orbital participation may be of minor importance in thiophene.) Structures similar to those shown in Fig. 5 can be written for the compounds

in series I and II (Fig. 6). The small but significant differences in barriers between corresponding compounds in series

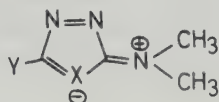


Fig. 6

I and II may then be explained if we assume that the structure shown in Fig. 6 has some importance when $X = S$ considering the possibility of the sulphur atom to participate with its 3d orbitals. When $X = O$ such valence-shell expansion is not possible. The sulphur heterocycle then has an extra possibility to stabilize (delocalize) negative charge donated by the dimethylamino group which may more than outweigh the greater electronegativity of the oxygen atom compared to sulphur. This will accordingly lead to an energetically more favourable initial state of the rotation process compared to the transition state in the 1,3,4-thiadiazole compounds than in the 1,3,4-oxadiazoles and thus to a higher barrier in the former compounds.

MacKenzie and MacNicol have estimated the barriers to rotation of the dimethylamino group in *N,N*-dimethyl-aniline and *p*-nitro-*N,N*-dimethyl-aniline to be 5.1 and 7.9 kcal/mol (ΔG_{133}^*), respectively³. The value at the same temperature for the nitro-substituted 1,3,4-oxadiazole Ia is 9.8 kcal/mol and the values for the corresponding 1,3,4-thiadiazoles are 7.5 (IIe) and 10.6 kcal/mol (IIa). A comparison of these values is not straightforward since they were determined from measurements in different solvents. Considering the quite large difference in the barrier values between the aniline derivatives and compounds Ia, IIa, and IIe it should, in spite of this restriction, be safe to conclude that the bonding interaction between the dimethylamino group and the ring, as it shows up in the height of the barriers, is significantly stronger in the two heterocyclic systems I and II than in the corresponding para substituted

N,N-dimethyl-anilines.

To study the influence of the para-substituent on the barriers in the aniline derivatives, MacKenzie and MacNicol plotted the barrier values given as $\Delta G^\ddagger_{133}$ against the Hammett σ^- values. The straight line obtained is reproduced in Fig. 7, line C.

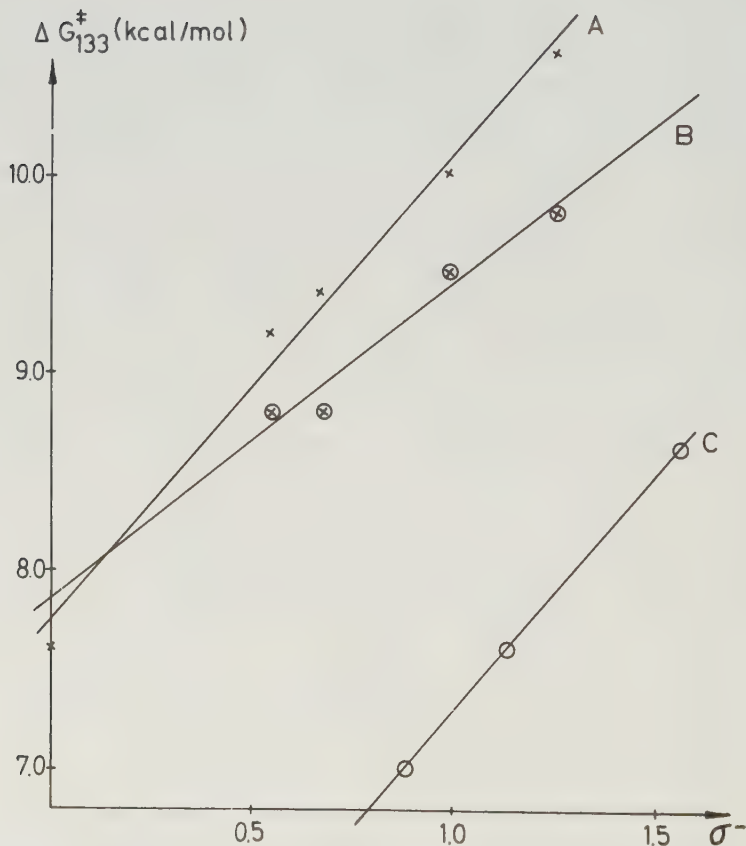


Fig. 7. Hammett correlations. Barriers $\Delta G^\ddagger_{133}$ vs. σ^- values.

This figure also shows corresponding plots representing the 1,3,4-oxadiazoles and -thiadiazoles in lines B and A, respectively. The values used are given in Table 8.

Table 8. Barrier values and σ^- values used in Fig. 7.

Compound	$\Delta G_{133}^{\ddagger}$ ^a (kcal/mol)	σ^- ^b
Ia	9.8	1.270
Ib	9.5	1.0
Ic	8.8	0.678
Id	8.8	0.55
IIa	10.6	1.270
IIb	10.0	1.0
IIc	9.4	0.678
IId	9.2	0.55
IIe	7.6	0.0

^aCalculated from Table 1 and 6.

^bValues from Ref. 60.

Excellent linear correlations were obtained in all cases. The correlation coefficients are 0.993, 0.981 and 1.000 (0.9999) for line A, B, and C, respectively. Line A and line C have almost the same slopes 2.32 and 2.29, respectively, showing a marked and almost identical influence of the substituents on the barriers in the 1,3,4-thiadiazole series II and in the N,N-dimethyl-anilines. This indicates that the electron relaying properties of the 1,3,4-thiadiazole ring and the benzene ring are very similar, at least when "para" positions are considered.

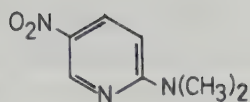
The slope of line B representing the 1,3,4-oxadiazoles is somewhat smaller, 1.53. It is interesting to note that using the

linear relationship between $\Delta G^\ddagger$ and σ^- in Fig. 7, the 5-unsubstituted 1,3,4-oxadiazole Ie is predicted to have a slightly higher barrier than the corresponding 1,3,4-thiadiazole IIe. Unfortunately, a very low coalescence temperature (< 154 K) prevented the experimental determination of the barrier in compound Ie. Considering the predicted relationship between the barriers in compounds Ie and IIe and the experimental results for compounds Ia-d and IIa-d which gives the reverse order of the barriers between series I and II, the explanation given above for the differences in the barriers between the two series based on Fig. 6 needs some additional discussion.

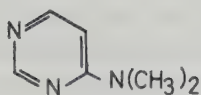
The crossing of line A and B in Fig. 7 and also the smaller slope of line B compared to line A may be rationalized without changing the conclusions drawn above based on 3d orbital participation, assuming a greater contribution of the resonance structure shown in Fig. 6 ($X = S$) with greater electron-withdrawing ability of the substituent Y, as measured by the σ^- constants. Such a rationalization is in line with suggestions that π -d interactions may be favoured by electron-withdrawing substituents causing an orbital contraction of the 3d orbitals^{61,62}. There is a great deal of controversy about the necessity of d orbital contraction in order to allow π -d bonding⁵⁴. A CNDO/2 study which will be presented later in the present work, supports the rationalization described above.

1,2,4-Thiadiazole and 1,2,3,4-thiatriazole

Katritzky and Tiddy⁴ have shown that the barriers to rotation of the dimethylamino group in 2-dimethylamino-5-nitropyridine and 4-dimethylaminopyrimidine are almost the same (Fig. 8). They found the result surprising; in view of the fact that the σ_R^O values, which should measure the resonance interaction, is 0.17 for the nitro group and 0.24 for a ring- α -a substituent.



$$\Delta H^\ddagger = 10.4 \pm 0.6 \text{ kcal/mol}$$



$$\Delta H^\ddagger = 10.7 \pm 0.4 \text{ kcal/mol}$$

Fig. 8

5-Dimethylamino-1,2,3,4-thiatriazole (IV) can be considered a ring-aza substituted 1,3,4-thiadiazole (IIe) or 1,2,4-thiadiazole (III) and then it may be concluded from Table 1 that the effect in this case is that expected from the σ_R^O values. Compound IV has a 1.4 kcal/mol higher barrier than the nitro substituted compound IIa.

Aza substitution of compound IIe raises the barrier ($\Delta H^\ddagger$) by 4.3 kcal/mol, but no effect on the barrier is found, when substitution is made in the 1,2,4-thiadiazole nucleus (Table 1). This difference may qualitatively be understood by consideration of the resonance structures in Fig. 9. No high probability



II e



III

Fig. 9

resonance structure can be written for the 1,2,4-system (III) with a negative charge on the carbon atom to be substituted by nitrogen. This should make the 1,2,4-thiadiazole barrier insensitive to substitution in this position compared to a compound in which the resonance theory description places a significant negative charge on the atom in question, as is the case in IIe.

Fig. 9 may also be used to explain the higher barrier of the 1,2,4-thiadiazole compound (III) compared to the 1,3,4-thiadiazole compound (IIe). In the former case the donated charge is distributed over two pyridine type nitrogens and on the basis of electronegativity this situation is more stabilized than when the charge is distributed over one pyridine nitrogen and one carbon atom as in IIe.

Entropies

The entropies of activation obtained in this work are consistently negative (Table 6). Deviations from $\Delta S^\ddagger \approx 0$ for a simple rotation process have often been viewed with scepticism and it has been argued that they may result from experimental errors⁴⁸. Instrumental and other sources of line broadening introduce, if they are not accounted for, systematic errors which give too high rate constants at slow exchange and too low at fast exchange and consequently too negative entropies. Problems connected with the determination of T_2 , especially at low temperatures, and insufficient knowledge of the temperature dependence of the chemical shift difference, $\delta\nu$, may also seriously affect the entropies of activation.

It is believed that all possible care to reduce uncertainties in the thermodynamic parameters has been taken in this work. In spite of this, the great sensitivity of $\Delta S^\ddagger$ to small systematic errors suggests that too much emphasis should not be placed on these values. It should, however, be noted that negative entropies of the same magnitude as those found in this

work have been obtained by Katritzky and Tiddy in their study of pyridines and pyrimidines⁴, and in recent work on carbamates⁶³. Negative entropies have also been found in measurements on N,N-dimethylanilines⁶⁴ and enamines⁶⁵.

The entropies for similar compounds can be assumed to be the same. This is supported by the almost identical values obtained for compounds Ib and IIa.

IV. MOLECULAR ORBITAL CALCULATIONS

IV.1 π -Electron model. The PPP approximation.

As mentioned in the introduction, the Pariser-Parr-Pople (PPP) approximation⁶⁶⁻⁶⁸ has been used in calculations that only consider the π -electrons of the molecules.

The PPP method is based on the Roothan equations⁶⁹ simplified by the Zero Differential Overlap (ZDO) approximation⁷⁰. The Fock-matrix elements in the PPP approximation are given by equations (10a) and (10b):

$$F_{\mu\mu} = H_{\mu\mu}^{\text{core}} - 1/2 q_{\mu} \gamma_{\mu\mu} + \sum_{\lambda} q_{\lambda} \gamma_{\mu\lambda} \quad (10a)$$

$$F_{\mu\nu} = \beta_{\mu\nu} - 1/2 p_{\mu\nu} \gamma_{\mu\nu}; \mu \neq \nu \quad (10b)$$

where $q_{\mu} = 2 \sum_i c_{i\mu}^2 = \pi$ -electron density at atom μ .

$p_{\mu\nu} = 2 \sum_i c_{i\mu} c_{i\nu} = \pi$ -bond order between atoms μ and ν .

the c 's are LCAO wave function coefficients.

$\gamma_{\mu\mu}$ = one-center repulsion integral.

$\gamma_{\mu\lambda}, \gamma_{\mu\nu}$ = two-center repulsion integrals (the sum in (10a) is taken over all atomic π -orbitals λ).

$\beta_{\mu\nu}$ = resonance integral.

The total π -electron energy is given by (11):

$$E_{\pi} = \sum_{\mu} q_{\mu} H_{\mu\mu}^{\text{core}} + 2 \sum_{\mu < \nu} p_{\mu\nu} \beta_{\mu\nu} + 1/4 \sum_{\mu} q_{\mu}^2 \gamma_{\mu\mu} + \sum_{\mu < \nu} (q_{\mu} q_{\nu} - 1/2 p_{\mu\nu}^2) \gamma_{\mu\nu} \quad (11)$$

According to Goeppert-Mayer and Sklar⁷¹ and with neglect of penetration integrals $H_{\mu\mu}^{\text{core}}$ can be written as:

$$H_{\mu\mu}^{\text{core}} = U_{\mu\mu} - \sum_{v \neq \mu} n_v \gamma_{\mu v} \quad (12)$$

Where n_v is the number of electrons contributed by the atomic orbital v . In this formulation $U_{\mu\mu}$ is treated as the negative ionization potential for atom μ ($-I_\mu$) in the appropriate valence state. According to an analysis of Fischer-Hjalmars⁷², $H_{\mu\mu}^{\text{core}}$ can also be formulated as:

$$H_{\mu\mu}^{\text{core}} = W_\mu - (n_\mu - 1)\gamma_{\mu\mu} - \sum_{v \neq \mu} n_v \gamma_{\mu v} \quad (13)$$

where W_μ is a parameter which includes the one-center part of the core Hamiltonian and penetration to neighbouring atoms.

The PPP method is mostly used as a semi-empirical method, which means that at least some of the integrals which appear in the Fock matrix (10a, 10b) are treated as parameters to be adjusted to give agreement between calculated and experimental properties of some chosen standard molecules. Two parametrization schemes, A and B, which have been used in this work, will now be described.

Parametrization scheme A

In this scheme formulation (12) was used to obtain values of $H_{\mu\mu}^{\text{core}}$, that is $H_{\mu\mu}^{\text{core}} = -I_\mu - \sum_{v \neq \mu} n_v \gamma_{\mu v}$. The appropriate I_μ values have been taken from Hinze and Jaffé⁷³. The two-center repulsion integrals $\gamma_{\mu v}$ were calculated by the Nishimoto-Mataga approximation⁷⁴. The one-center repulsion integrals were evaluated according to formula (14) proposed by Pariser⁷⁵.

$$\gamma_{\mu\mu} = I_\mu - A_\mu \quad (14)$$

where A_μ is the electron affinity of atom μ . The A_μ values were

taken from the above mentioned work of Hinze and Jaffé. Values for the resonance integrals $\beta_{\mu\nu}$ were calculated by formula (15) suggested by Kon⁷⁶.

$$\beta_{\mu\nu} = \frac{k_{\mu\nu} |\cos \theta|}{r_{\mu\nu}^6} \quad (15)$$

Here $k_{\mu\nu}$ is a constant calibrated from UV data of small standard molecules^{76,77}. For non-neighbouring atoms $k_{\mu\nu}$ is assumed to be zero. $r_{\mu\nu}$ is the distance in Å between atoms μ and ν , and θ is the rotation angle from a coplanar geometry, which in this work is used to describe the rotation of the dimethylamino group. The values for I_μ , $\gamma_{\mu\mu}$ and $k_{\mu\nu}$ used in parametrization scheme A are summarized in Table 9.

Parametrization scheme B

This scheme was suggested by Roos and Skancke⁸⁰, and is based on a theoretical investigation of the ZDO approximation by Fischer-Hjalmars⁷².

In the latter paper it is concluded that the W_μ parameter in (13) should be made dependent on the surroundings of the atom μ in order to obtain the same order of approximation in the different parameters. In most previous studies W_μ has been assumed constant for the same kind of atom. In this scheme W_μ is given by (16)

$$W_\mu = W_\mu^O + \sum_\nu \{ \Delta W_\mu^O(\nu) + \delta_{\mu\nu}^W (R_{\mu\nu} - R_{\mu\nu}^O) \} \quad (16)$$

where the sum is a correction to W_μ^O due to nearest neighbours. R and R^O are bond lengths. The parameters $\gamma_{\mu\nu}$ and $\beta_{\mu\nu}$ for nearest neighbours are evaluated from formulas (17) and (18):

$$\gamma_{\mu\nu} = \gamma_{\mu\nu}^0 + \delta_{\mu\nu}^{\gamma} (R_{\mu\nu} - R_{\mu\nu}^0) \quad (17)$$

$$\beta_{\mu\nu} = \beta_{\mu\nu} + \delta_{\mu\nu}^{\beta} (R_{\mu\nu} - R_{\mu\nu}^0) \quad (18)$$

W_{μ}^0 , $\Delta W_{\mu}^0(v)$, $\delta_{\mu\nu}^W$, $\gamma_{\mu\nu}^0$, $\delta_{\mu\nu}^{\gamma}$, $\beta_{\mu\nu}^0$ and $\delta_{\mu\nu}^{\beta}$ are determined empirically from experimental ionization potentials and electronic transitions of a few standard molecules. The one-center repulsion integrals $\gamma_{\mu\mu}$ are evaluated from spectral data, and the two-center integrals $\gamma_{\mu\nu}$ for non-neighbours are calculated using the hard sphere approximation according to Parr⁸¹. For non-neighbours $\beta_{\mu\nu}$ is assumed to be zero. Numerical values for the parameters are summarized in Table 10.

In some of the calculations the hyperconjugative effect of methyl groups has been included. This is done according to Roos⁸², Groppen and Skancke⁸³. The parameters are included in Table 10.

Table 9. Parameters according to scheme A.

Atom	I_{μ} (eV)	$\gamma_{\mu\mu}$ (eV)
C (sp^2)	11.16	11.13
C (sp)	11.19	11.09
$\dot{N}$ (sp^2)	14.12	12.34
$\dot{N}$ (sp)	14.18	12.52
$\ddot{N}$ (sp^2)	28.59	16.63
S (sp^2)	22.88 ^a	11.90 ^a
$\dot{O}$ (sp^2)	17.70	15.23
$\ddot{O}$ (sp^2)	33.90 ^a	18.60 ^a

^aCalculated from the promotion energies of Hinze and Jaffé by Dewar et al.^{78,79}.

Bond	k (eV)
CC	-17.464
C $\dot{N}$	-13.983
C $\ddot{N}$	-11.579
CS	-35.091
C $\dot{O}$	-8.8086
C $\ddot{O}$	-12.129
NN	-12.167
S-N	-37.743
CN (cyano)	-6.475
NO (nitro)	-9.572

Table 10. Parameters for scheme B (eV).

Atom	W_{μ}^O	$\gamma_{\mu\mu}$	Bond $\mu-\nu$	$\beta_{\mu\nu}^O$	$\gamma_{\mu\nu}^O$	$\delta_{\mu\nu}^W$	$\delta_{\mu\nu}^{\beta}$	$\delta_{\mu\nu}^{\gamma}$	$\Delta W_{\mu}^O(\nu)$	$\Delta W_{\nu}^O(\mu)$	$R_O(\text{\AA})$	Ref.
C	-9.84	11.97	C-C	-2.42	6.91	9.22	3.05	-3.99	0.07	0.07	1.397	82
$\dot{N}$	-12.57	15.44	C- $\dot{N}$	-2.72	7.16	5.6	2.6	-3.99	0.03	0.14	1.338	84
$\ddot{N}$	-8.52	15.44	C- $\ddot{N}$	-2.25	6.34	5.6	2.6	-3.99	0.03	0.14	1.338	84
S	-10.62	9.58	C-S	-1.37	7.28	9.22	3.05	-3.99	-0.70	0	1.714	85
$\dot{O}$	-19.60	18.89	C- $\dot{O}$	-2.46	9.33	0	0	0	-0.71	0	1.22	86
$\ddot{O}$	-11.18	18.89	C- $\ddot{O}$	-1.80	6.20	0	0	0	-0.09	1.51	1.35	87
(C)-CH ₃	-12.02	10.01	C-CH ₃	-1.38	5.70	0	0	0	0.50	0	1.70 ^a	82
($\ddot{N}$)-CH ₃	-12.02	10.01	$\ddot{N}$ -CH ₃	-1.33	5.65	9.22	3.05	-3.99	0.23	0	1.70 ^a	83
			$\dot{N}$ - $\dot{N}$	-2.67	9.00	9.22	3.05	-3.99	-0.32	-0.32	1.33	83
			$\ddot{N}$ - $\dot{N}$	-2.67	9.00	9.22	3.05	-3.99	-0.06	-0.32	1.33	83
N(nitro)	-8.52	15.43										88
O(nitro)	-19.80	18.89	N-O	-2.37	9.25	0	0	0	-0.32	0	1.208	88

^aThe methyl orbital is replaced by two tangent spheres with a methyl carbon - tangent point distance = 0.18 Å.

IV.2 All valence electron model. The CNDO/2 approximation.

The CNDO/2 approximation, developed by Pople, Santry and Segal^{89,90}, considers all σ - and π -electrons in the valence shell. "Inner shell" electrons are neglected. A brief presentation of the most important formulas will be given here. A book written by Pople and Beveridge gives a more detailed treatment of the approximations leading from the Roothan equations to the Complete Neglect of Differential Overlap (CNDO) approximation⁹¹. The Fock matrix elements in the CNDO/2 approximation are given by equations (19a) and (19b).

$$F_{\mu\mu} = -1/2(I_{\mu} + A_{\mu}) + [(P_{AA} - Z_A) - 1/2(P_{\mu\mu} - 1)]\gamma_{AA} + \sum_{B \neq A} (P_{BB} - Z_B)\gamma_{AB} \quad (19a)$$

$$F_{\mu\nu} = 1/2(\beta_A^O + \beta_B^O)S_{\mu\nu} - 1/2 P_{\mu\nu}\gamma_{AB} \quad (19b)$$

where I_{μ} = valence state ionization potential

A_{μ} = valence state electron affinity

P_{AA} = total electron density on atom A

$P_{\mu\mu}$ = electron density of orbital μ

Z_A = the core-charge on atom A

γ_{AA} = repulsion integral for two electrons on atom A

γ_{AB} = repulsion integral for one electron on atom A and one on atom B

β_A^O = resonance integral due to atom A. (The total resonance integral β_{AB}^O is made up of contributions from two atoms, A and B; $\beta_{AB}^O = 1/2(\beta_A^O + \beta_B^O)$).

$S_{\mu\nu}$ = overlap integral = $\int \chi_{\mu} \chi_{\nu} d\tau$ where χ_{μ} and χ_{ν} are atomic orbitals

The repulsion integrals γ_{AA} and γ_{AB} , as well as the overlap integrals $S_{\mu\nu}$ are calculated using Slater orbitals. In the calculations of γ_{AA} and γ_{BB} only S-type orbitals are used:

$$\gamma_{AA} = \int S_A^2(1) \frac{1}{R_{12}} S_A^2(2) d\tau_1 d\tau_2$$

$$\gamma_{AB} = \int S_A^2(1) \frac{1}{R_{12}} S_B^2(2) d\tau_1 d\tau_2$$

where R_{12} is the distance between electrons 1 and 2. The values used for the parameters I and A are taken from spectral data for atoms. The β^O -parameters have been chosen to give the best fit between CNDO calculations and ab initio calculations on small molecules. The parameter values are summarized in Table 11.

Table 11. Parameters used in CNDO/2 calculations (eV).

Atom	C	N	O	S	H
1/2 ($I_s + A_s$)	14.051	19.316	25.390	17.650	7.176
1/2 ($I_p + A_p$)	5.572	7.275	9.111	6.989	
1/2 ($I_d + A_d$)				0.713	
- β_A^O	21.000	25.000	31.000	18.150	9.000

The total energy in the CNDO/2 approximation is given by (20).

$$E = \sum_A E_A + \sum_{A<B} E_{AB} \quad (20)$$

$$\text{where } E_A = \frac{1}{2} \sum_{\mu\nu}^{\text{AA}} (P_{\mu\mu} P_{\nu\nu} - \frac{1}{2} P_{\mu\nu}^2) \gamma_{\text{AA}}$$

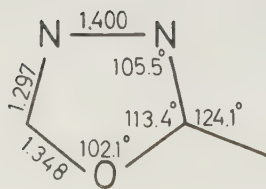
$$\text{and } E_{\text{AB}} = \sum_{\mu\nu}^{\text{AB}} (2P_{\mu\nu} \beta_{\text{AB}}^{\text{O}} S_{\mu\nu} - \frac{1}{2} P_{\mu\nu}^2 \gamma_{\text{AB}}) + (Z_A Z_B R_{\text{AB}}^{-1} - P_{\text{AA}} Z_B \gamma_{\text{AB}} - \\ - P_{\text{BB}} Z_A \gamma_{\text{AB}} + P_{\text{AA}} P_{\text{BB}} \gamma_{\text{AB}})$$

The core repulsion between atoms has been included by means of the expression $\frac{Z_A Z_B}{R_{\text{AB}}}$.

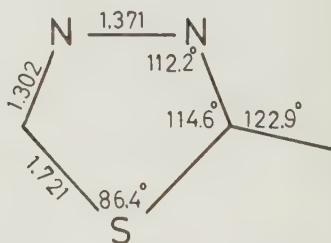
Calculations were made with and without 3d-orbitals on sulphur using the spd- and sp-models due to Santry and Segal⁹⁰.

IV.3 Geometries used in the calculations

Bond angles and bond lengths for the 1,3,4-oxadiazole and -thiadiazole ring system were taken from microwave determinations^{77,92}. The values are reproduced in Fig. 10.



I

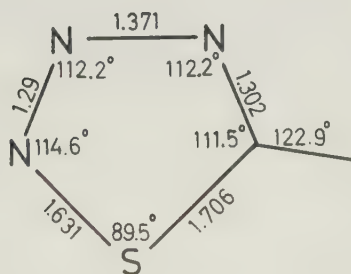


II

Fig. 10

The outer angle in I, 124.1° , was estimated from the corresponding angle in II. (After this work was completed, the full microwave analysis of I was published⁹³. According to this analysis, the outer angle should be 128.5° .) The values in Fig. 10 are assumed to be unchanged by substitution.

Since no microwave determination of the structures of the ring systems III-VI exist, their geometries had to be constructed from related compounds. The 1,2,3,4-thiatriazole nucleus in IV was constructed from the geometry of the 1,3,4-thiadiazole ring (II) assuming a S-N bond length of 1.631 Å. This is the value found for the S-N bond length in 1,2,5-thiadiazole⁹⁴. The N_3-N_4 bond was kept at 1.371 Å while the N_2-N_3 bond length was given a value of 1.29 Å. The SNN, NNN, and NNC angles were taken to be identical to the corresponding angles in the 1,3,4-thiadiazole nucleus. Starting from the above assumed values, the remaining bond angles and bond lengths can be calculated. The 1,2,4-thiadiazole ring structure in III was constructed from the 1,2,3,4-thiadiazole geometry determined above by simply changing the nitrogen atom at position 3 to a carbon atom. The ring geometry of compound IV is given in Fig. 11.



IV

Fig. 11

The ring structures in the 1,2,4-triazole and tetrazole series, V and VI, respectively, were taken from calculated values obtained by Roche from an iterative procedure using the "LCAO ameliorée" method⁹⁵. The validity of this procedure has been tested by comparing calculated and experimental bond angles and bond lengths for a number of five-membered nitrogen heterocycles. The comparison showed good agreement between calculated and experimental values and it was concluded that the procedure can be used with reliability to calculate geometries of five-membered nitrogen heterocycles. The geometries used in the present work are given in Fig. 12.

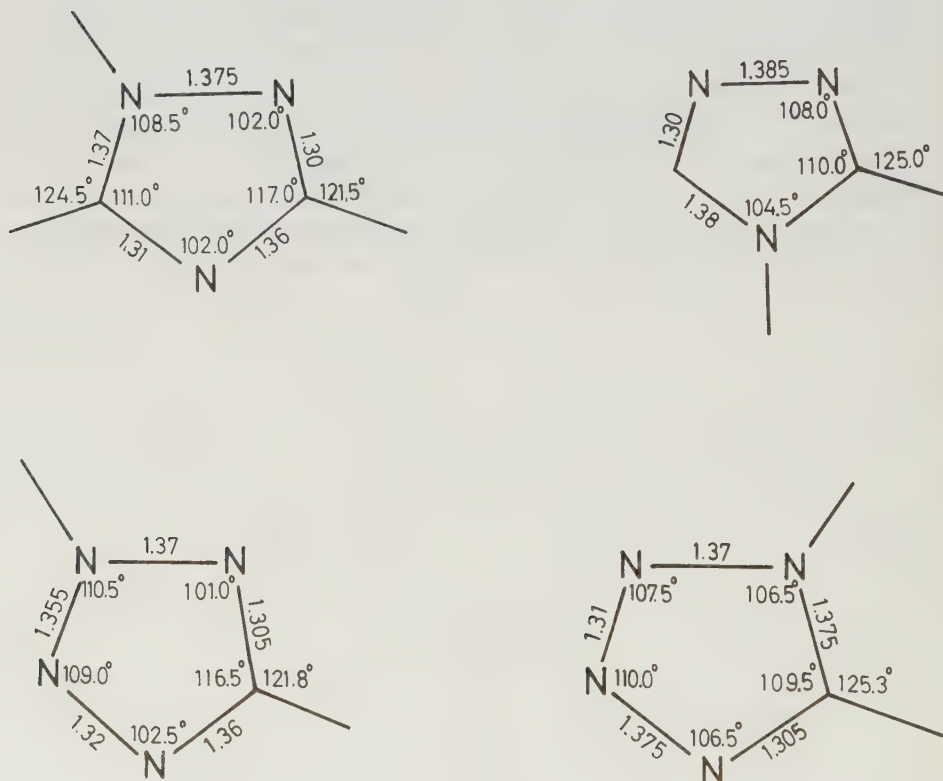
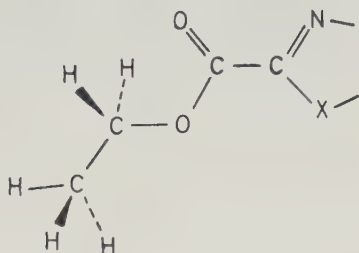


Fig. 12

The geometries of the substituents Y were constructed from values in Ref. 96 and are summarized in Table 12.

The carbon-nitrogen bond lengths in the dimethylamino group were assumed to be 1.46 Å and the carbon-hydrogen bond length 1.08 Å. Since the CNC bond angles in the dimethylamino group were varied, these angles will be specified later.

All ring systems considered in this work are assumed to be planar. The substituents NO_2 , CN, and C_6H_5 were fixed in a conformation in which the substituent Y and the ring system are coplanar. The conformation used in the calculations for the carboethoxy substituent is shown below.



Test calculations using other reasonable conformations showed no significant changes in calculated molecular properties considered in this work. The trifluoromethyl substituent was maintained in a conformation where two fluor atoms and the heteroatom X are staggered.

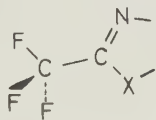


Table 12. Geometries of the substituents Y.

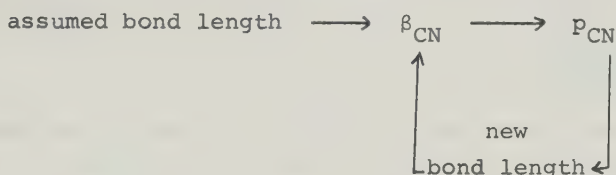
Y	Bond distances in Å		Bond angles	
NO ₂	C(ring)-N	1.49	C-N-O	118°
	N-O	1.21	O-N-O	124°
CN	C(ring)-C	1.42		
	C-N	1.16	C-C-N	180°
CO ₂ C ₂ H ₅	C(ring)-C	1.48	O-C-O	122°
	C=O	1.23	C-C=O	121°
	C-O	1.31	C-C-O	117°
	CH ₂ -O	1.51	C-O-CH ₂	117°
	CH ₂ -CH ₃	1.55	all other angles	109.47°
	C-H	1.08		
CF ₃	C(ring)-C	1.52	all angles	109.47°
	C-F	1.33		
H	C(ring)-H	1.08		
C ₆ H ₅	C(ring)-C	1.45		
	C-C	1.397	all angles	120°
	C-H	1.08		

The exocyclic carbon-nitrogen bondlength.

Since the calculated barriers are expected to be significantly sensitive to the exocyclic carbon-nitrogen bond length, it was found necessary to use a geometrical optimization procedure in this case. The procedure used in the PPP calculations is different from that used in the CNDO/2 calculations so the two procedures will be described separately.

The PPP procedure

The exocyclic carbon-nitrogen bond length to be used in the PPP calculations was determined by an iterative procedure⁸⁴:



A new bond length was calculated from the bond order obtained from a calculation with a guessed bond length. Formulas (21)⁹⁷ and (22)⁸⁴ were used to calculate the bond length R .

$$R = 1.448 - 0.178 p_{CN} \quad (\text{scheme A}) \quad (21)$$

$$R = 1.458 - 0.18 p_{CN} \quad (\text{scheme B}) \quad (22)$$

Different formulas were used in the two parametrization schemes A and B since formula (22) is exclusively connected with scheme B.

The iteration was continued until there was no significant change in the bond lengths in two consecutive calculations. In calculations using scheme A the iterations were continued until convergence was obtained within three decimal places. In calcu-

lations with scheme B the CN bond length was only iterated to two decimal places, since this scheme was mainly used to calculate UV transitions, which proved to be only slightly affected by changes in the exocyclic carbon-nitrogen bond length. The resulting bond lengths are given in Table 13. No calculations were made for compounds III and IV using scheme B since parameters for the S-N bond are not available in this scheme.

The CN bond lengths of the transition state for the rotation of the dimethylamino group, where this group is rotated 90° out of the plane of the ring, were assumed to be the same as those shown in Table 13, since there is no way to use the iterative procedure in the transition state, where according to formula (15) $\beta_{\text{CN}} = 0$ ($\theta = 90^\circ$) and consequently $p_{\text{CN}} = 0$.

The CNDO/2 procedure

The exocyclic carbon-nitrogen bond lengths for compounds Ia-f, IIa-f, Va and VIa, which are the only compounds considered in the CNDO/2 calculations, were obtained in the following way. The CNC bond angles were kept at 120° , corresponding to a "planar" dimethylamino group. Two compounds in each of the series I and II: Ia, Ie, IIa, and IIe were chosen, representing the extremes of electron-withdrawing capacity among the substituents under consideration. For the initial state of the rotation process, where the dimethylamino group and the heterocyclic ring are coplanar, energy values for at least five different C-N bond lengths were calculated. Parabolas were least-squares fitted to the energy vs. bond length plot, beginning with the three points of lowest energy and then expanding by including next neighbour points. This method makes it possible to select a variation range where parabolic approximation is reasonable. The bond lengths that minimized the total energies were evaluated and adopted as bond lengths for the initial state of the rotation. To minimize the computational work a mean value of the bond lengths for compounds Ia and Ie was calculated and

Table 13. Exocyclic carbon-nitrogen bond lengths used in the PPP calculations.

Compound	Scheme A (Å)	Scheme B (Å)
Ia	1.404	1.40
Ib	1.404	1.40
Ic	1.405	1.40
Ie	1.406	1.40
If	1.406	1.40
IIa	1.403	1.39
IIb	1.404	1.39
IIc	1.404	1.39
IIe	1.405	1.39
IIIf	1.405	1.39
III	1.404	-
IV	1.404	-
Va	1.405	1.40
Vc	1.401	1.40
Vd	1.400	1.40
Ve	1.405	1.40
VIa	1.405	1.40
VIb	1.403	1.40

used throughout series I and the same procedure was followed in series II. This procedure is reasonable since, as can be seen in Table 14, where the results are summarized, the differences in the optimal bond lengths for Ia and Ie and for IIa and IIe are very small. The same procedure was used to determine the bond lengths in the transition state of the rotation. The results are given in Table 14, and an example of the energy vs. bond length plots obtained by this procedure is given in Fig. 13. The bond lengths for compounds Va and VIa were obtained in the same way.

It is very satisfying that this procedure predicts a longer bond for the transition state than for the initial state, as expected from the qualitative valence bond description of the two states.

Table 14. Exocyclic carbon-nitrogen bond lengths obtained by the CNDO/2 procedure.

Compound	Optimal CN-distance (Å)	
	initial state	transition state
Ia	1.375	1.387
Ie	1.379	1.389
IIa	1.370	1.388
IIe	1.374	1.390
Mean value series I	1.377	1.388
Mean value series II	1.372	1.389
Va	1.390	1.400
VIa	1.390	1.400

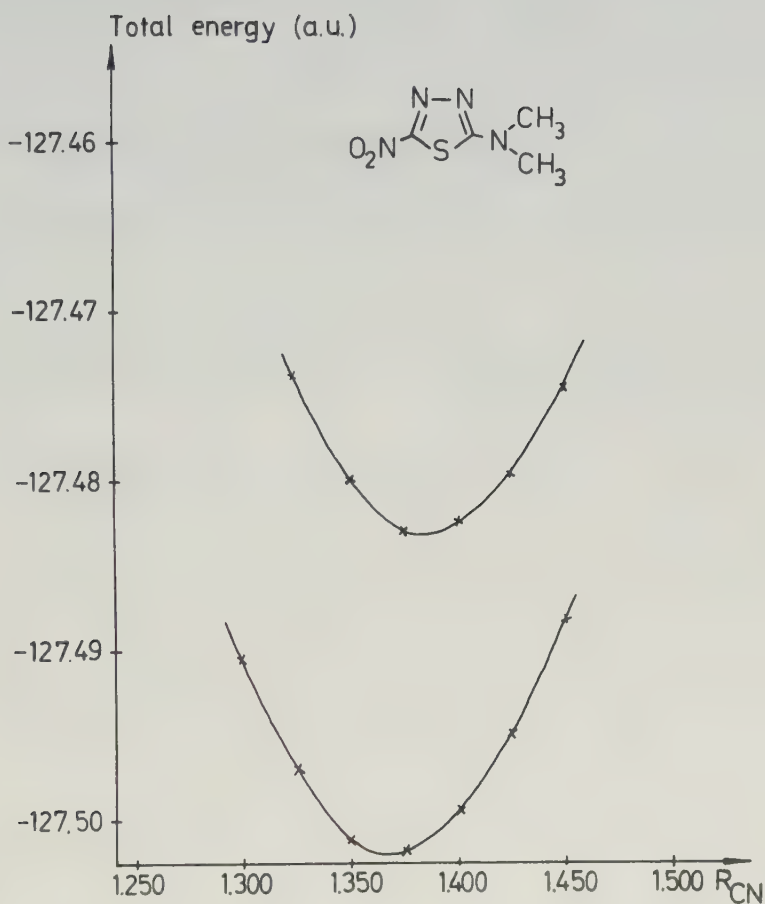


Fig. 13. Total energy vs. bond length plot for compound IIa.

Programs

The programs for the PPP calculations were written by Prof. Rolf Manne, University of Bergen, Norway (used for Scheme A) and Dr. Marianne Sundbom, Institute of Theoretical Physics, University of Stockholm (used for Scheme B).

A standard CNDO/2 program⁹¹ was used for the all-valence-electron calculations, except for those performed with the sp-approximation for sulphur, in which case a revised CNDO/2 program was employed⁹⁸. The calculations were performed on a UNIVAC 1108 computer.

IV.4 General considerations in comparisons between experimental and calculated barriers

The proper thermodynamic parameter to be compared with values from quantum chemical calculations is the enthalpy of activation ($\Delta H^\ddagger$). However, it must be borne in mind that the calculated barriers refer to gas phase values, while the experimental barriers in this work have been measured in solution. Very little is known about the differences in barriers to internal rotation in the gas phase and solution or liquid phase. Harris and Spragg⁹⁹ measured the barrier to rotation of the dimethyl-amino group in dimethylnitrosamine, in both gas and liquid phases. They found the barrier ($\Delta G_T^\ddagger$) to be ca. 2 kcal/mol lower in the gas phase than in the liquid^C phase. Approximately the same difference between gas and liquid phase has been found in far-infrared measurements of the rotational barrier in benzaldehyde¹⁰⁰. (Recently, Drakenberg and Lehn¹⁰¹ found that the inversion barriers in tertiary amines are almost the same in the gas phase and in an inert solvent.)

The few data available make it impossible to estimate the corrections that may be necessary in accurate comparisons between experimental and theoretical values. However, for a

series of related compounds these corrections can be assumed to be constant, and thus at least barrier differences can be compared with a high degree of reliability, while comparisons between "absolute" calculated and experimental values must be done with caution.

IV.5 Results of the PPP calculations

The barriers to internal rotation of the dimethylamino group calculated by the PPP method using parametrization scheme A are given in Table 15 which also includes the experimental $\Delta H^\ddagger$ values reproduced from Table 1. Only compounds with substituents contributing π -electrons to the system have been included in the calculations. Thus compounds with a methyl or trifluoromethyl substituent have been omitted. No hyperconjugation has been taken into account.

The calculated barrier values are given as the difference in π -electron energy between the transition state (the dimethylamino group rotated 90° out of the plane of the ring) and the initial state (dimethylamino group and ring system coplanar).

The calculated values are quite close to the experimental ones, especially for compounds with electron-withdrawing substituents (a, b, and c). Even if the possible sources of errors discussed above are considered, the calculated changes in π -energy between the transition state and the initial state of the rotation process in most cases satisfactorily accounts for the magnitude of the barriers.

The calculations also satisfactorily reproduce the order of the barriers in series I and II, and give the correct order of the barriers between corresponding compounds in the two series, for which experimental barriers could be determined. The experimental observation that the 1,2,4-thiadiazole III has a higher barrier than the isomeric 1,3,4-thiadiazole IIe is reproduced by the calculations. The calculated difference between compounds III and IIe is, however, much smaller than the experimental one. Similarly ring aza substitution in compound

Table 15. Barriers to internal rotation of the dimethylamino group in compounds Ia-VIb calculated by the PPP method using parametrization scheme A.

Compound	Calculated barrier (kcal/mol)	$\Delta H^\ddagger$ experimental (kcal/mol)
Ia	9.1	8.4
Ib	8.9	8.1
Ic	8.8	7.4
Ie	8.6	<6.1
If	8.5	<6.1
IIa	9.3	9.1
IIb	9.0	8.6
IIc	9.0	8.0
IIe	8.7	6.2
IIIf	8.7	6.1
III	9.1	10.5
IV	8.9	10.5
Va	8.9	-
Vc	9.6	-
Vd	10.0	-
Ve	8.9	-
VIa	8.9	-
VIb	9.4	-

IIf to give compound IV experimentally results in an increase of the barrier, which is also shown in the calculations, but again the calculations underestimate the difference.

Underestimation of barrier differences is a general trend in the calculations. This is clearly seen in the calculated barrier differences between the different substituted compounds in series I and II. For instance, the experimental difference in the barriers for compounds IIa and IIf is 2.9 kcal/mol, but the calculated difference is only 0.6 kcal/mol. It can be suspected that the neglect of changes in the σ -skeleton between the transition state and initial state of the rotation at least partly may be responsible for this underestimated sensitivity of the barriers to substitution. As will be seen later, inclusion of valence shell σ -electrons (CNDO/2 approximation) results in a more correct picture of the influence of the substituents on the barriers.

Another factor which may be involved is the way in which the resonance integrals $\beta_{\mu\nu}$ are evaluated. As mentioned previously, these integrals were obtained from calibrations using UV data for some standard molecules. In principle calibrations should be made from ground state data if ground state properties are to be calculated¹⁰². However, very few such calculations have been done and no scheme is available which includes all the atoms and bonds in the compounds considered in the present work.

A few calculations were carried out using parametrization scheme B, but no improvement was obtained. For instance, the differences in barriers between compounds IIa and IIf were still calculated to 0.6 kcal/mol.

The calculated barriers to dimethylamino group rotation in the sterically unhindered 1,2,4-triazole and tetrazole, Va and VIa, respectively, are 8.9 kcal/mol for both. The calculated values, corresponding to $\Delta H^\ddagger$, are not easily translated into a prediction of the height of the barriers since a value of 8.9 kcal/mol in the other calculations corresponds to experimental values between 8.1 and 10.5 kcal/mol (Table 15). By using entropies in the same range as those found experimentally for compounds Ib, IIa, III, and IV (Table 6), the calculations

indicate that the ΔG^*_T 's for compounds Va and VIa are at least as large as ΔG^*_T for ^Ccompound IIe. The failure to observe exchange broadening of the dimethylamino signal in the NMR spectra of the former compounds then probably depends on too small shifts ($\delta\nu_0$) leading to lower coalescence temperatures than was possible to obtain. This point will be further discussed in connection with the CNDO/2 calculations.

The calculated barriers using a hypothetical planar initial state conformation of compounds Vc, Vd, Ve, and VIb are in most cases significantly higher than those calculated for Va and VIa. There is no reason to believe that the shifts between the dimethylamino signals in these compounds are so small that they alone could account for the unobserved splitting of the dimethylamino group NMR signal in these cases. Steric interaction between the ring methyl group and the dimethylamino group leading to an increased energy of the initial state of the rotation and a consequent lowering of the barrier is a more plausible explanation.

Charge densities and bond orders

The purpose of the work presented in this section was to investigate the possibility of obtaining useful relations between calculated charge densities and bond orders on the one hand, and experimental barriers on the other. Such results would be useful in the sense that the relations may help to predict barriers to internal rotation. Conclusions and explanations based on charge densities and bond orders have also been compared to conclusions and explanations made on the basis of qualitative resonance theory.

Charge densities

Charge densities obtained from the PPP calculations for the 5-unsubstituted compounds in series I and II, as well as for

compounds III and IV, are shown in Fig. 14.

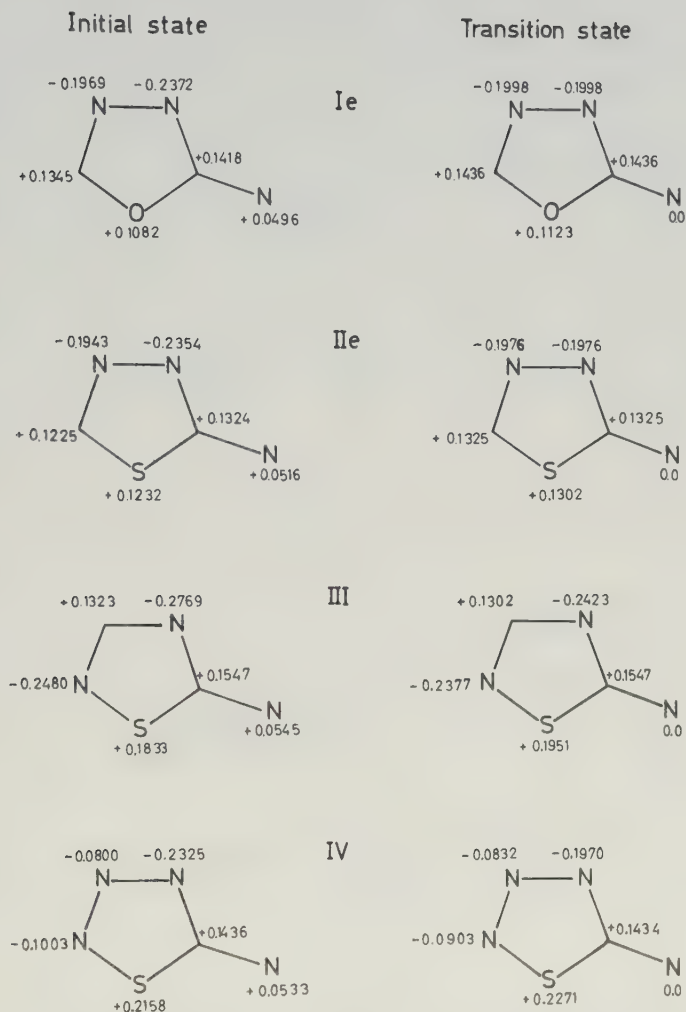


Fig. 14. Charge densities from PPP calculations.

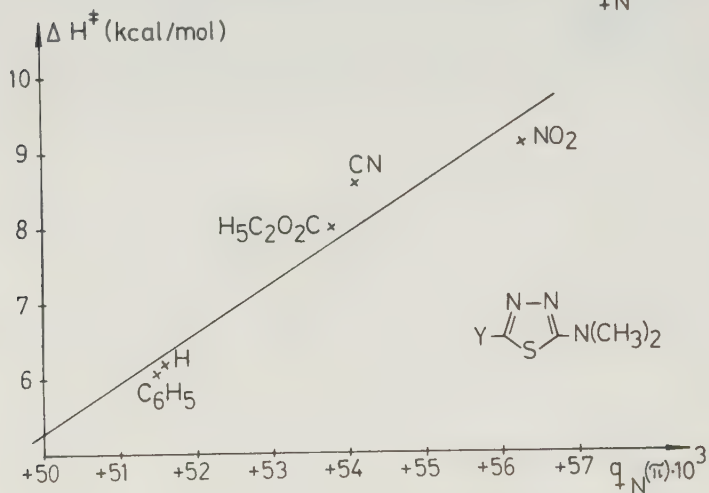
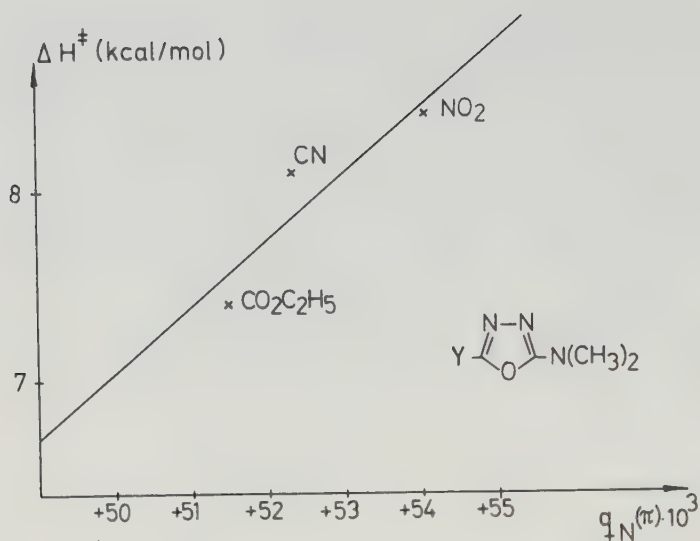


Fig. 15. Nitrogen charge ($q_N(\pi)$) vs. barrier plots from PPP calculations.

According to the calculations, the exocyclic nitrogen atom donates negative charge to the ring system in the initial state of the rotation process. The influence of the substituents on the initial state in series I and II is to make the dimethylamino nitrogen more positive with increasing electron-withdrawing ability of the substituent (as measured by the Hammett σ^- -values (Table 8)). This effect on the nitrogen charge is related to the substituent effect on the experimental barriers, as can be seen in Fig. 15, where a rough linear relationship between the nitrogen charges $q_N(\pi)$ and the experimental barriers is demonstrated.

The nitrogen charge vs. barrier plot for series I can be used to predict the barriers for compounds Ie and If for which no experimental barriers could be determined. The nitrogen charges in these compounds are + 0.0497 and + 0.0496 respectively, and a least-squares fit of the three points of series I in Fig. 15 gives a straight line from which $\Delta H^\ddagger$ values of 7.0 and 6.9 kcal/mol for Ie and If, respectively, can be obtained. The predicted value for Ie is close to that predicted from the Hammett plot in Fig. 7 (6.5 kcal/mol).

The relations shown in Fig. 15 are in accord with the qualitative resonance theory picture, which assumes an increasing importance of structures summarized in Fig. 16 with increasing electron-withdrawing capacity of the substituent Y, and an accordingly higher barrier to the dimethylamino rotation

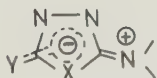


Fig. 16

with increasing positive charge on the exocyclic nitrogen.

The phenyl group is π -electron-donating according to the calculations, while the other substituents are π -electron-withdrawing, as can be seen in Table 16, where Δ is the

difference in charge between initial state and transition state.

Table 16. Group π -electron densities.

Group	Series I			Series II		
	Initial state	Transition state	Δ	Initial state	Transition state	Δ
NO ₂	-0.0104	-0.0092	-0.0012	-0.0125	-0.0110	-0.0015
CN	-0.0146	-0.0114	-0.0032	-0.0182	-0.0149	-0.0033
CO ₂ C ₂ H ₅	-0.0215	-0.0195	-0.0020	-0.0245	-0.0221	-0.0024
C ₆ H ₅	+0.0178	+0.0204	-0.0026	+0.0165	+0.0194	-0.0029

According to the resonance theory, it would be expected on the basis of the structure shown in Fig. 17 that the negative

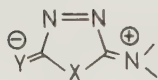


Fig. 17

charge accepted by the substituent should parallel the electron donation from the exocyclic nitrogen atom, and also that the barrier to rotation should parallel the accepted negative charge on the substituent. As can be seen in Table 16 the calculations give another picture. The "lone pair" electron donation in the initial state affects the substituent charge densities to a very small extent and the substituent influence on the exocyclic nitrogen charge and on the barrier, which is in the order NO₂ > CN > CO₂C₂H₅ > C₆H₅, does not parallel the electron density difference on the substituents between the initial state

and the transition state (Δ in Table 16). This means that the predominant effect of the substituents is a polarization of the electron distribution in the ring system in such a way, that a delocalization of the exocyclic nitrogen "lone pair" into the ring is facilitated. The effectiveness of this polarization then follows the order $\text{NO}_2 > \text{CN} > \text{CO}_2\text{C}_2\text{H}_5 > \text{C}_6\text{H}_5$.

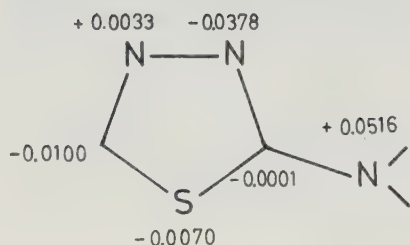
The difference in charge densities on the oxygen atoms in series I and the sulphur atom in series II, between the initial state and the transition state of the dimethylamino group rotation is given in Table 17. (The minus sign means that the atom in question is more negatively charged in the initial state than in the transition state.)

Table 17. Differences in charge densities on the oxygen atom in series I and the sulphur atom in series II between initial state and transition state.

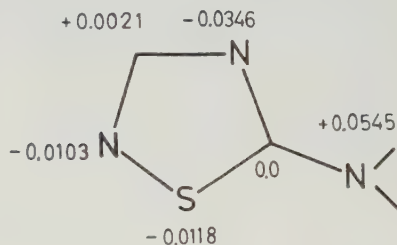
Series	a	b	c	e	f
I	-0.0043	-0.0041	-0.0040	-0.0041	-0.0039
II	-0.0079	-0.0074	-0.0072	-0.0070	-0.0068

From the table it is clear that sulphur accepts more negative charge than oxygen. The barrier differences between series I and II can then be understood in terms of the better ability of the 1,3,4-thiadiazole ring to delocalize the exocyclic nitrogen "lone pair" through the better ability of the sulphur atom to accept negative charge. This is surprising in view of the greater electronegativity of oxygen compared to sulphur. It is also seen that the π -charge on sulphur is more sensitive than the π -charge on oxygen to the substituent in 5-position. This is in qualitative accord with the observation made earlier, that plots of barriers vs. the Hammett σ^- -constants (Fig. 7) give a greater slope for series II than for series I.

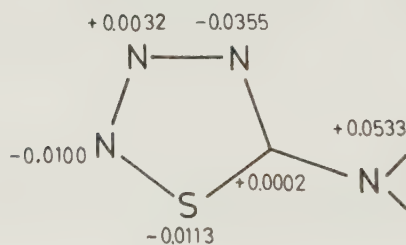
It is interesting to compare the delocalization of the exocyclic nitrogen "lone pair" in compounds IIe, III, and IV, as measured by the PPP charge density differences between initial state and transition state in these compounds. The values are given in Fig. 18.



IIe



III



IV

Fig. 18

The electron distributions in the three compounds are very similar, and the higher barrier of III and IV ($\Delta H^\ddagger = 10.5$ kcal/mol for both) compared to Ie ($\Delta H^\ddagger = 6.2$ kcal/mol) can be understood considering the greater electronegativity of nitrogen compared to carbon. Aza substitution in IIe to give IV takes place at a carbon atom that gains negative charge on going from transition state to initial state, and the better ability of nitrogen to stabilize such a charge lowers the initial state energy and raises the barrier. The lack of influence of aza substitution on the barrier in III is then a consequence of the very small change in charge density, between initial and transition state, on the carbon atom to be substituted. The same type of reasoning can be applied to explain the barrier difference between compounds IIe and III. Fig. 18 also shows that a higher barrier is accompanied by more negative charge accepted by the sulphur atom.

The electron density picture of the barrier differences between compounds IIe, III, and IV given above supports the qualitative picture based on valence bond structures presented earlier in this work.

Bond orders

The bond order of the bond around which the rotation is hindered has often been used as a measure of the height of the rotational barrier. It has been argued that the bond order measures the double bond character of the bond in question and that a high degree of double bond formation will give rise to a high barrier¹⁰³. However, this reasoning is affected by a theoretical weakness, since the bond order in the transition state is by definition zero in all compounds, if the resonance integral β_{CN} is set equal to zero in the transition state of the rotation process. We are thus in practice comparing an initial state property (p_{CN}) with an energy difference between transition state and initial state ($\Delta H^\ddagger$), but this procedure

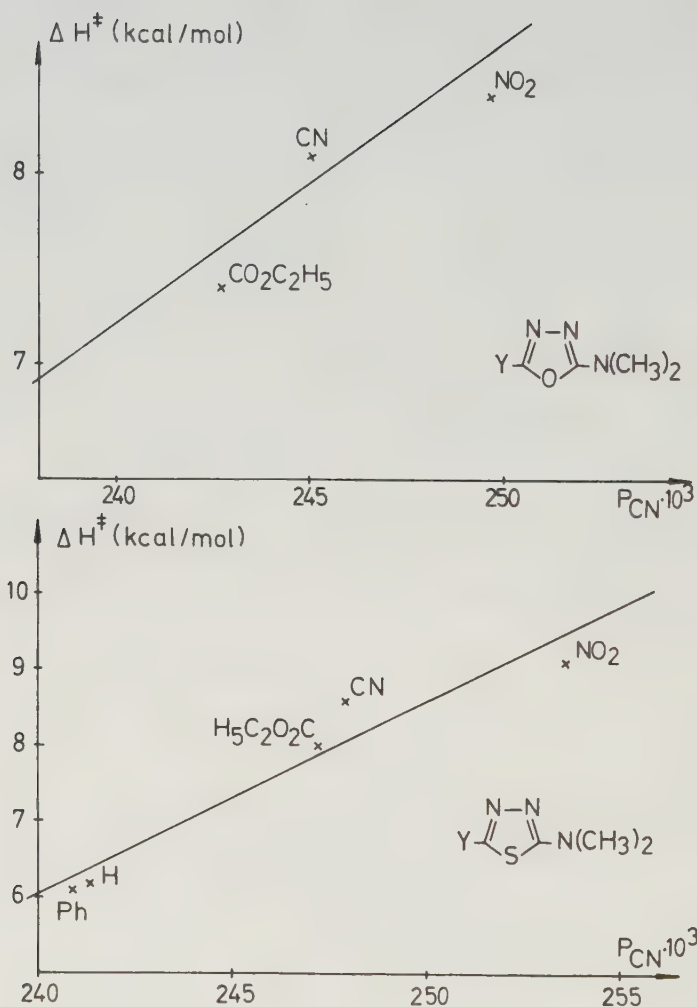


Fig. 19. Exocyclic carbon-nitrogen bond order (p_{CN}) vs. rotational barrier ($\Delta H^\ddagger$).

may not be a serious approximation if only related compounds are considered. The similar results obtained by the present calculations and the CNDO/2 calculations presented later, where differences in π -bond order between different compounds in the transition state are accounted for, support this conclusion.

Fig. 19 gives plots of p_{CN} vs. $\Delta H^\ddagger$ for the rotation of the dimethylamino group. The plots demonstrate a linear relationship between barriers and calculated bond orders with a greater bond order corresponding to a higher barrier.

The striking similarities between the plots in Fig. 19 and Fig. 15 indicate that an increasing positive charge on the exocyclic nitrogen atom corresponds to a higher double bond character of the exocyclic carbon-nitrogen bond. This is expected from valence bond structures such as:



The barriers for compounds Ie and If can be predicted to 6.9 kcal/mol for both from Fig. 19 and the calculated bond orders, 0.2380 and 0.2376, respectively. These barrier values are almost identical to those obtained from the nitrogen charge vs. barrier plot in Fig. 15.

IV.6 Results of the CNDO/2 calculations.

The CNDO/2 calculations have been restricted to compounds Ia-f, IIa-f, Va and VIa. The investigation includes the effect of sulphur 3d-orbitals on the calculated barriers of compounds IIa-f and a study of the influence of different geometries around the exocyclic nitrogen atom.

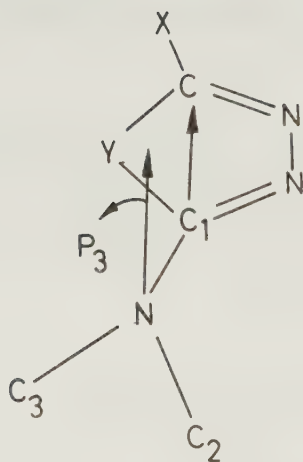
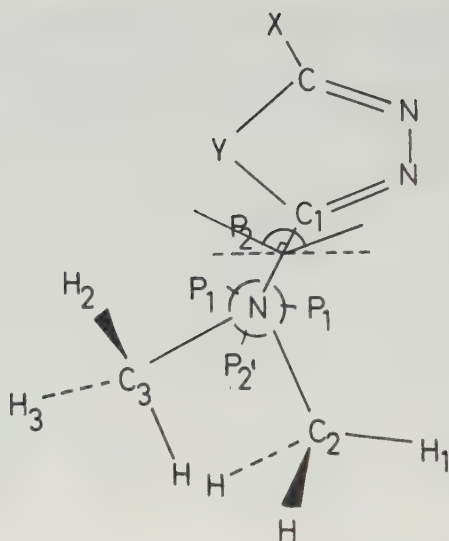


Fig. 20. Definition of the parameters used in the description of the geometry and rotation of the dimethylamino group (Y = O, S).

Since different bond angles around the amino nitrogen were used in the calculations, these angles are given as parameters shown in Fig. 20.

P1 and P2' are bond angles in the dimethylamino group, and P2 is the angle between the planes through C_1NC_2 and C_1NC_3 . P3 is the angle between a plane perpendicular to the ring and a plane through C_1N and bisecting the C_2NC_3 angle. P3 describes the rotation of the dimethylamino group.

The two methyl groups were kept in the staggered conformation shown in Fig. 21a, with bond angles of 109.47° .

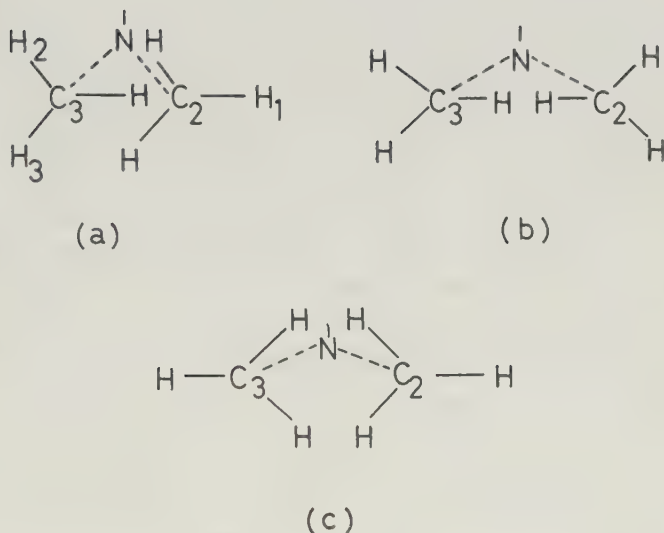


Fig. 21. The methyl group conformations of the dimethylamino group used in the energy calculations.

This is the simplest conformation to treat when P2 is given different values, since the "cog-wheel" situation is then preserved. However, this conformation may not correspond to the state with lowest energy^{6,10}. To obtain an estimate of the error introduced by adopting the "cog-wheel" conformation, calculations were made with $P_1 = 120^\circ$, $P_2 = 180^\circ$, $P_3 = 0^\circ$ and with the methyl groups in two other reasonable conformations, shown in Figs. 21b and 21c. Compared to the "cog-wheel" conformation, that shown in Fig. 21b destabilizes the molecule by 0.8 kcal/mol, while that in Fig. 21c leads to a stabilization by 0.5 kcal/mol. The latter conformation, however, introduces problems with H-H interactions when P2 is varied, and to avoid an excess of computational work with different methyl rotamers, the small energy difference was neglected and the staggered conformation (Fig. 21a) was used throughout the calculations.

Calculations with a "planar" dimethylamino group

The rotational barriers for compounds Ia-f and IIa-f were calculated for $P_1 = 120$ and $P_2 = 180^\circ$ (the planar model, Fig. 20). The barriers are given as the differences between the total energies for $P_3 = 90$ and $P_3 = 0^\circ$. To investigate the importance of sulphur 3d-orbital on the calculated barriers in compounds IIa-f, calculations were made with (spd model) and without (sp model) 3d-orbitals on sulphur. The results are given in Table 18, which also includes the experimental barriers.

For one of the compounds, Ib, the total energy was calculated for several different values of P3 using an exocyclic carbon-nitrogen bond length of 1.383 Å (the mean value of the bond lengths for $P_3 = 0$ and $P_3 = 90^\circ$, see Table 14). The resulting curve is shown in Fig. 32. Identical energy maxima are found for $P_3 = 90$ and $P_3 = 270^\circ$, and minima are found for $P_3 = 0$ and $P_3 = 180^\circ$. The difference between the energy values for $P_3 = 0$ and $P_3 = 180^\circ$ is negligible. The potential curve shows the validity of using $P_3 = 0^\circ$ as initial state and $P_3 = 90^\circ$ as transition state for the rotation.

Table 18. Calculated and experimental barriers.
 "Planar" dimethylamino group model.

Compound	spd-model kcal/mol	sp-model kcal/mol	experimental $\Delta H^\ddagger$ kcal/mol
Ia		8.0	8.4
Ib		7.2	8.1
Ic		7.2	7.4
Id		7.4	7.4
Ie		6.5	<6.1
If		6.0	<6.1
IIa	12.1	7.7	9.1
IIb	10.8	6.7	8.6
IIc	11.2	7.3	8.0
IId	11.6	7.1	7.8
IIe	10.2	6.3	6.2
IIIf	10.0	6.1	6.1
Va		6.7	
VIa		6.1	

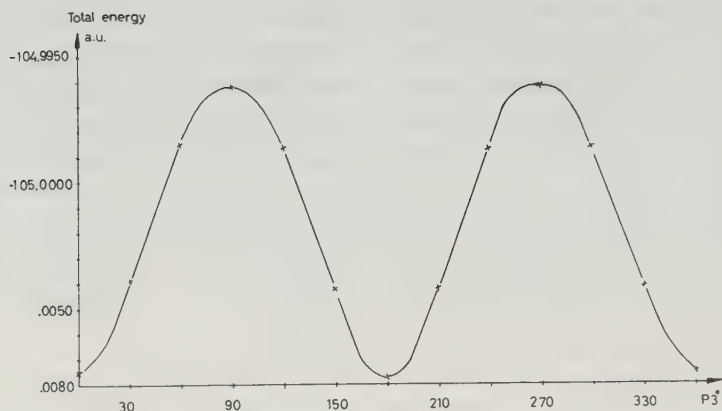


Fig. 22. Potential curve for the rotation of the dimethylamino group in Ib ($P_1 = 120^\circ$, $P_2 = 180^\circ$, and $R(\text{CN}) = 1.383 \text{ \AA}$).

The simple model used in the calculations accounts surprisingly well for the barriers (Table 18). The calculated barriers for compounds Ia-f are very close to the experimental ones, while the experimental values for the sulphur compounds (IIa-f) generally lie between those calculated by the two extreme models (the sp and spd models). A comparison between the calculated and experimental barrier values must be made with caution, considering, for instance, that in these calculations the possibility of different geometries around the amino nitrogen in the initial state and in the transition state has been neglected. A brief study of the effect of pyramidalisation of the dimethylamino nitrogen group will be given later.

However, the errors introduced by this simplification may to a first approximation be considered constant throughout a series of related molecules.

The ability of the CNDO/2 method to reproduce experimental substituent effects should be discussed with reference to the 5-unsubstituted compounds (Ie and IIe). Unfortunately, the barrier in Ie is too low to be measured, but instead a value of 6.5 kcal/mol was used, obtained from the least-squares plot of the barriers in Ia-Id vs. the corresponding Hammett σ^- -constants (Fig. 7). The barrier differences relative to these references are given in Table 19. The general trends of the substituent effects are satisfactorily reproduced by the calculations, but the calculated changes are in general smaller than the experimental ones, which means that the substituent effects are in general somewhat underestimated. This may reflect a deficiency of the CNDO/2 method to adequately treat conjugation effects, as has been proposed by Ljunggren and Wettermark¹⁰⁵ and as well as by Gropen and Seip¹⁶. The cyano substituted compounds (Ib, IIb) show a particularly serious underestimation of the substituent effect. This is in line with earlier observations, which show that the CNDO/2 approximation underestimates the electron-withdrawing ability of the cyano group^{106,107}. This underestimation is more serious in the initial than in the transition state and leads to a too low barrier.

The CNDO/2 calculations give a much more realistic picture of the substituent effects than the π -electron calculations presented earlier (Table 15). This indicates that inclusion of valence σ -electrons may be necessary to obtain a correct theoretical description of systems similar to those studied in this work.

The effect of 3d-orbitals

It has been observed that inclusion of 3d-orbitals in the basis set of sulphur affects various calculated molecular

Table 19. Changes in barriers relative to Ie and IIe.

Compound	spd-model kcal/mol	sp-model kcal/mol	experimental kcal/mol
Ia		+1.5	+1.9
Ib		+0.7	+1.6
Ic		+0.7	+0.9
Id		+0.9	+0.9
Ie		0	0
If		-0.5	-
IIa	+1.9	+1.4	+2.9
IIb	+0.6	+0.4	+2.4
IIc	+1.0	+1.0	+1.8
IId	+1.4	+0.8	+1.6
IIe	0	0	0
IIIf	-0.2	-0.2	-0.1

properties to different degrees. Thus, in calculations on thiophene, Clark⁵⁸ has shown that charge densities and the dipole moment are significantly affected by inclusion of 3d-orbitals, while the total calculated energy is much less sensitive. However, rotational barriers are generally very small compared to the total energy and small deviations in the stabilizing effect of the 3d-orbitals between the initial state and the transition state may result in significant changes in the calculated barriers.

Table 18 shows that the inclusion of 3d-orbitals on sulphur increases the barriers by about 4 kcal/mol. The calculations on compounds IIa-f without 3d-orbitals (sp model) fail to reproduce the experimental order of the barriers between series I and II. Using the spd model, the correct order is obtained, but the differences are exaggerated. The compounds in series II have 0.4-0.7 kcal/mol higher experimental barriers than the corresponding compounds in series I. The spd model gives differences in the range 3.6-4.2 kcal/mol between the two series.

In Table 18 it is interesting to note that when the sp model is used, the deviations from the experimental values are greatest for compounds with electron-withdrawing substituents (IIa-d), while when the spd model is used the deviation between calculation and experiment is greatest for compounds IIe and IIf. This means that it may be more important to include d-orbitals in calculations involving electron-withdrawing substituents than when the substituents are, for instance, hydrogen and phenyl which are electron-donating according to the calculations. This is in line with conclusions drawn earlier in this work on the basis of a correlation between barriers and σ^- -constants (Fig. 7). The observation may be interpreted as d-orbital participation made favourable by orbital contraction due to the electron-withdrawing substituents^{61,62}.

It is also to be noted that the use of the sp model in the calculations of the rotational barriers in compounds IIa-f,

predicts compound Ie to have a slightly higher barrier than compound IIe, supporting the conclusions drawn from the Hammett plots in Fig. 7.

The addition of 3d-orbitals on sulphur stabilizes the initial state ($P3 = 0^\circ$) as well as the transition state ($P3 = 90^\circ$). Table 20 gives the differences between the calculated total energies obtained by the sp model and those obtained by the spd model. The table shows that the initial states are stabilized by about 4 kcal/mol more than the transition states. The increase in the barriers on addition of 3d-orbitals to sulphur in compounds IIa-f is thus the result of a relatively more stabilized initial state. The exaggerated stabilization may be a consequence of the too contracted d-orbitals obtained by the spd model used⁹⁰.

Compounds Va and VIa

The calculated barriers for compounds Va and VIa, 6.7 and 6.1 kcal/mol, respectively, are close to the values calculated for compounds Ie-f and IIe-f (sp-model, Table 18). This suggests, in agreement with conclusions made on the basis of PPP calculations, that the reason for the failure to observe hindered rotation in the NMR spectra of the former compounds is that the shifts, $\delta\nu_0$, in Va and VIa are significantly smaller than that found for compound IIe (28.8 Hz), since the coalescence temperature for IIe is close to the lowest possible temperature which can be obtained by the apparatus and solvent used.

Effects of a pyramidal dimethylamino group

When studying barriers to internal rotation with quantum chemical methods, the choice of structural parameters to be optimized is always a point of discussion. Similar techniques for selecting parameters to be varied, applied to different molecules, may affect the calculated barriers to a varying

Table 20. Differences in total energy between the sp- and spd-model.

Compound	P3	Difference sp-spd kcal/mol
IIa	0°	185.9
IIa	90°	181.5
IIb	0°	187.8
IIb	90°	183.7
IIc	0°	187.3
IIc	90°	183.4
IId	0°	187.6
IId	90°	183.1
IIe	0°	186.1
IIe	90°	182.2
IIf	0°	189.3
IIf	90°	185.4

degree, due to the properties of the calculation method used¹⁰⁸.

In this work geometrical optimization of the carbon-nitrogen bond around which the rotation takes place has been assumed to be important. An equally important structural parameter, the pyramidalicity of the dimethylamino group, will now be discussed. Pyramidal arrangement of the amino group in aromatic amines is well known from experiments^{109,110} and theory¹¹¹.

Compound Ib was selected for this study. The exocyclic CN-bond length was kept fixed at 1.383 Å as in Fig. 22. The parameters P1 and P2 (Fig. 20) were varied simultaneously and their optimal values were found to within $\pm 5^\circ$. This was done for three values of P3. The results are given in Table 21.

Table 21. Optimal pyramidalicity values for compound Ib.

P1	P2	P2'	P3	Total energy a.u.	Stabilization energy relative to planar case a.u.
100°	115°	112.3°	90°	-105.0215	0.0254
105°	115°	109.1°	-90°	-105.0136	0.0174
110°	120°	108.9°	180°	-105.0164	0.0088

Optimization leads in all cases to significant stabilization compared to the planar model. The optimal values for P1 and P2 for the different values of P3 are quite similar. The large deviation from a planar geometry when P3 = 180° is unexpected and casts doubt on the validity of the pyramidalization procedure. To study this further, a common pyramidal situation, P1 = 107.5 and P2 = 117.5°, was selected and the total energy

was calculated for several values of P_3 . The resulting curve is shown in Fig. 23. Not only has the amplitude of the curve

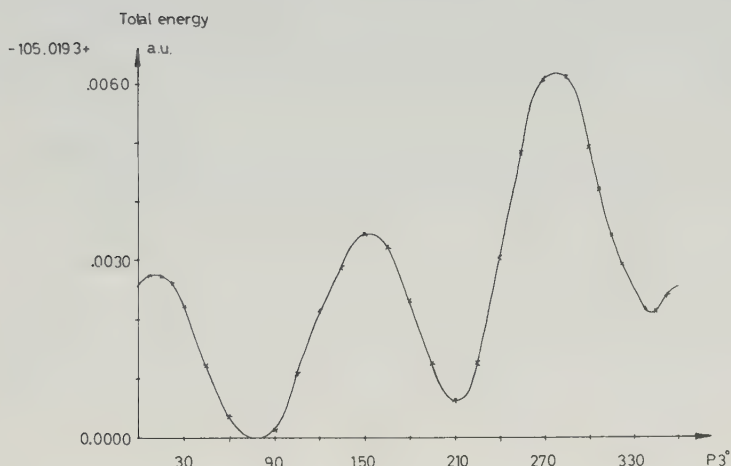


Fig. 23. Potential curve for the rotation of the dimethyl-amino group in Ib ($P_1 = 107.5^\circ$, $P_2 = 117.5^\circ$ and $R(\text{CN}) = 1.383 \text{ \AA}$).

decreased compared to the planar case (Fig. 22), but the shape of the curve is quite changed, and is now no longer in accord with experiment. The potential curve displays three minima with different energy values. The detailed shape is to some extent an artefact of the fixed staggered conformation of the methyl groups. By allowing them to change freely between the two possible staggered conformations, two minima will obtain the same energy and the third one will be moved from 75° to 90° . However, the NMR lineshape will be that of a three-site case where two sites have the same population but the third a different one, and this is in complete disaccord with the

experimental results, which show exchange between two equally populated sites.

An attempt to analyze the effect of pyramidalization was made in the following way. With P1 fixed at 120° , three potential curves were constructed corresponding to P2 = 180, 160, and 140° , and with P3 stepped in 30° intervals from 0 to 360° (Figs. 24, 25, and 26 (X)). Two effects are apparent: the total energy decreases, and the energy of the potential maximum at P3 = 90° decreases more rapidly than that at P3 = 270° .

An attempt has now been made to resolve the different contributions to the barrier, using the technique of a truncated Fourier expansion¹¹². The following contributions have been assumed: 1. Non-bonded interactions between the three "outer" hydrogen atoms (H₁, H₂, and H₃ in Fig. 2a) and the oxygen and nitrogen atoms in the ring. These are three one-fold barriers with different phase angles. The latter are calculated from the assumed geometry of the molecule. 2. Interaction between the "lone pair" of the dimethylamino nitrogen and the π -orbitals of the ring (n - π interaction). This is a two-fold barrier.

These interactions are assumed to be described by cosine functions of the angle P3 = X, e.g. (23) for the interaction between H₂ and N,

$$V_{NH} = 1/2 V_{NH}^0 [1 - \cos(X + \phi_2)] \quad (23)$$

where ϕ_2 is the phase angle. The expression (24) is obtained for the total energy.

$$\begin{aligned} V(X) = & 1/2 V_{NH}^0 [2 + K_N - K_N \cos(X + \phi_1) - \cos(X + \phi_2) - \\ & \cos(X + \phi_3)] + 1/2 V_{OH}^0 [2 + K_O + K_O \cos(X + \phi_1) + \cos(X + \phi_2) \\ & + \cos(X + \phi_3)] + 1/2 V_{el}^0 (1 - \cos 2X) \end{aligned} \quad (24)$$

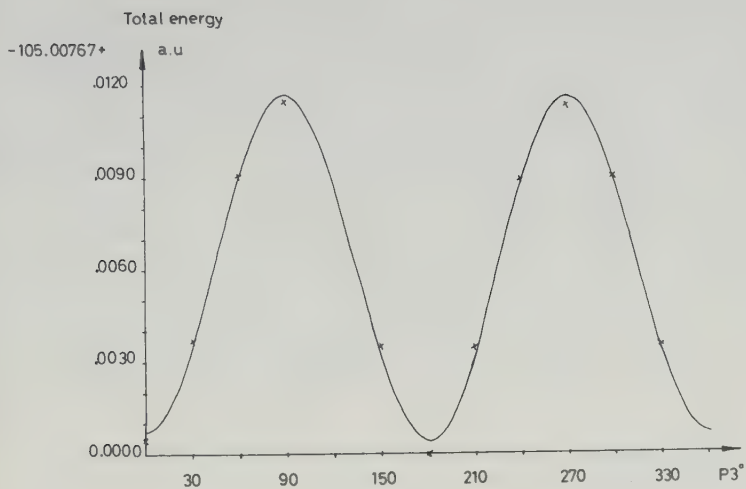


Fig. 24. CNDO/2 energy values (x) and Fourier curve (—) for Ib as a function of P_3 ($P_1 = 120^\circ$, $P_2 = 180^\circ$).

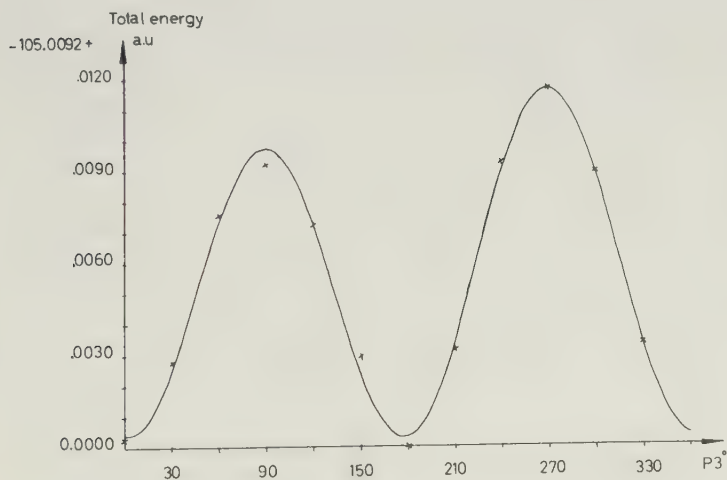


Fig. 25. CNDO/2 energy values (x) and Fourier curve (—) for Ib as a function of P_3 ($P_1 = 120^\circ$, $P_2 = 160^\circ$).

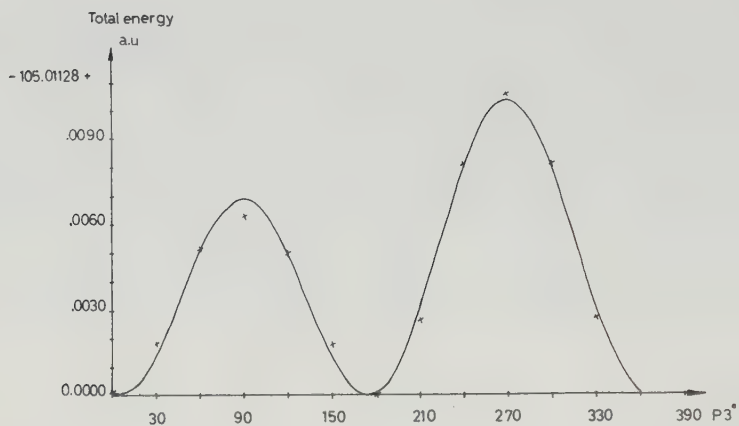


Fig. 26. CNDO/2 energy values (x) and Fourier curve (—) for Ib as a function of P_3 ($P_1 = 120^\circ$, $P_2 = 140^\circ$).

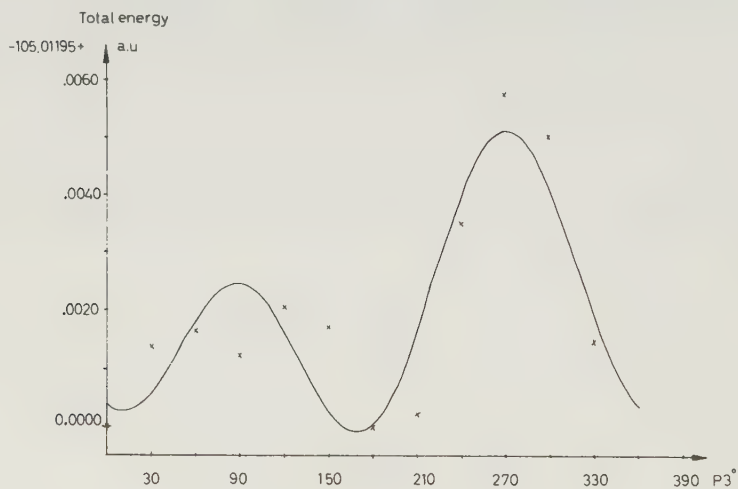


Fig. 27. CNDO/2 energy values (x) and Fourier curve (—) for Ib as a function of P_3 ($P_1 = 110^\circ$, $P_2 = 140^\circ$).

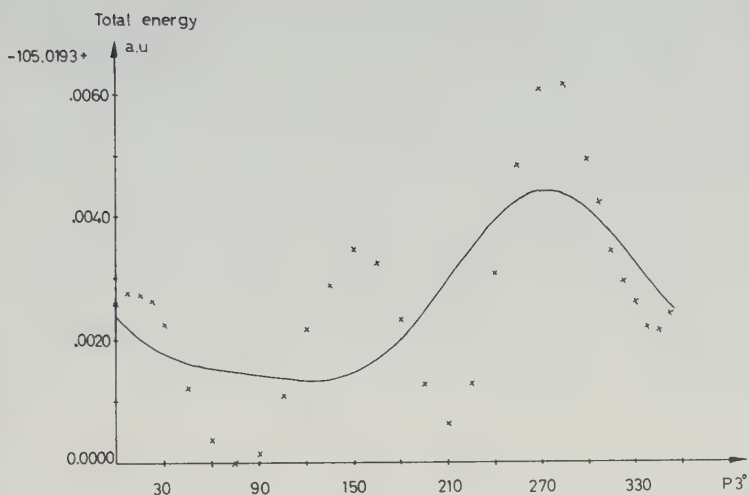


Fig. 28. CNDO/2 energy values (x) and Fourier curve (—) for Ib as a function of P_3 ($P_1 = 107.5^\circ$, $P_2 = 117.5^\circ$).

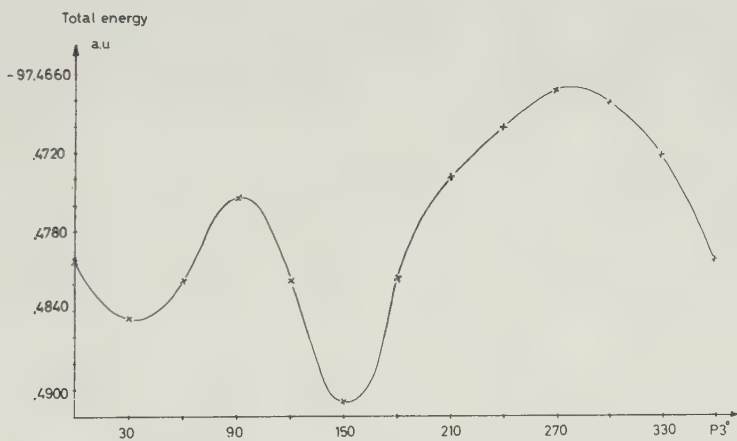


Fig. 29. Potential curve for the rotation of the dimethyl-amino group in IIb ($P_1 = 107.5^\circ$, $P_2 = 117.5^\circ$, $R(\text{CN}) = 1.381 \text{ \AA}$).

Here V_{el}^O is the contribution from n- π interaction for $X = 90^\circ$ and K_O and K_N are scaling factors to account for the fact that H_1 is closer to the ring atoms than H_2 and H_3 . V_{NH}^O , V_{OH}^O , and V_{el}^O were obtained by least-squares fitting of curves, calculated by (24) for selected pairs of K_N and K_O , to the appropriate CNDO/2 potential curves. K_N and K_O were stepped, and the resulting two-dimensional maps were examined for regions of minimum energy. These regions are extremely shallow, but by comparing different maps it was possible to select reasonable values for K_N and K_O . The resulting curves are shown in Figs. 24, 25, and 26, and the corresponding K_N and K_O and V_O^O values in Table 22.

Table 22. Coefficients from truncated Fourier expansion.

Fig.	Parameter values		Coefficients found by stepping and least-squares technique				
	P1	P2	K_O	K_N	$10^4 \cdot V_{OH}^O$	$10^4 \cdot V_{NH}^O$	$10^4 \cdot V_{el}^O$
24	120°	180°	1.0	1.0	3.6	0.33	110
25	120°	160°	2.0	1.7	-14	17	100
26	120°	140°	2.0	1.7	-13	15	8.5
27	110°	140°	2.0	2.0	-10	11	36
28	107.5°	117.5°	2.1	2.1	-2.1	13	7.3

The fit between the curves calculated by CNDO/2 and expression (24) is quite good, and from V_{el}^O values the following conclusions can be drawn. For $P1 = 120$, $P2 = 180^\circ$ the n- π interaction is of paramount importance for the shape of the potential curve, and the values of K_N and K_O are without effect.

Analysis of the CNDO/2 curves for $P_2 = 160$ and 140° shows a gradually diminishing contribution from $n-\pi$ interaction and an increase in hydrogen-nitrogen and hydrogen-oxygen interaction. The latter appears as an attraction in the pyramidal cases, which is the main reason for the unsymmetrical shape of the potential curves. The decreasing $n-\pi$ interaction with increasing pyramidity of the nitrogen atom is in agreement with the qualitative picture, but the attraction between oxygen and hydrogen even at very short distances is unexpected and alarming. The results suggest that such interactions may increasingly dominate the CNDO/2 picture of the rotation with increasing pyramidity of the dimethylamino group. Attempts to fit the model function to the case where $P_1 = 110$ and $P_2 = 140^\circ$ as well as to the "optimal" pyramidal case with $P_1 = 107.5$ and $P_2 = 117.5^\circ$, were unsuccessful. It is clear from Figs. 27 and 28 that no acceptable approximation could be obtained. It seems that the two maxima emerging in the region $P_3 = 0-210^\circ$ make an approximation impossible.

Working with the hypothesis that the model function is not fundamentally wrong, the above behaviour might be explained if the cosine functions do not simulate non-bonded interactions when the distances are small (down to 2 Å in this case). Perhaps more peaked functions should be used. Attempts to explain the two maxima using simple functions simulating Coulomb interactions were also unsuccessful.

To further elucidate the hydrogen-oxygen interactions we calculated the potential curve for the corresponding sulphur compound (Ib) with $P_1 = 107.5$ and $P_2 = 117.5^\circ$ using the spd model. The result given in Fig. 29 shows a more "normal" curve with at least qualitatively the expected behaviour. Also in this case, however, it was impossible to reproduce the CNDO/2 curve by a function of type (24).

Conclusions

From the above it is apparent that only the model with a planar nitrogen atom in the dimethylamino group can reproduce

the experimental barriers. With this model, on the other hand, the agreement is remarkably good. When allowance is made for a pyramidal structure of the dimethylamino group, the agreement breaks down, and in the optimized structure the potential curve is quite unrealistic. A somewhat similar case is found in a CNDO/2 calculation on formamide¹⁵, for which the planar model gives good numerical agreement with the experimental barrier, but the model with a planar initial state but a pyramidal transition state accounts only for about half of the experimental barrier. These results are probably due to a shortcoming of the CNDO/2 method, since at least in the transition state a pyramidal structure seems reasonable.

An analysis of the pyramidal case indicates that the failure is due to an underestimation of the repulsion between non-bonded atoms by the CNDO/2 method. This allows a too close mutual approach of the methyl groups, as well as of the methyl groups and the ring oxygen and nitrogen atoms. The interaction between the oxygen and hydrogen atoms appears as a binding contribution even at the closest approach, at a distance of about 2 Å. The sum of the van der Waals radii of these atoms is 2.72 Å, and at 2.0 Å a 6-12 Lennard Jones potential¹¹³ gives a repulsion of 4.2 kcal/mol. This leads to an incorrect scaling of resonance and steric effects. Dewar and Kohn¹¹⁴ conclude from calculations on barriers in amides by the MINDO/2 method that only a procedure which explicitly includes one-center overlap, e.g. the NDDO method, can satisfactorily account for barriers where lone pairs are involved. This is substantiated by recent calculations on formic acid by the CNDO/2 and NDDO methods¹¹⁵.

Charge densities and bond orders

Total and π -charge densities for the 5-unsubstituted compounds Ie and IIe obtained by the CNDO/2 calculations are given in Fig. 30. (N-methyl groups have been omitted.)

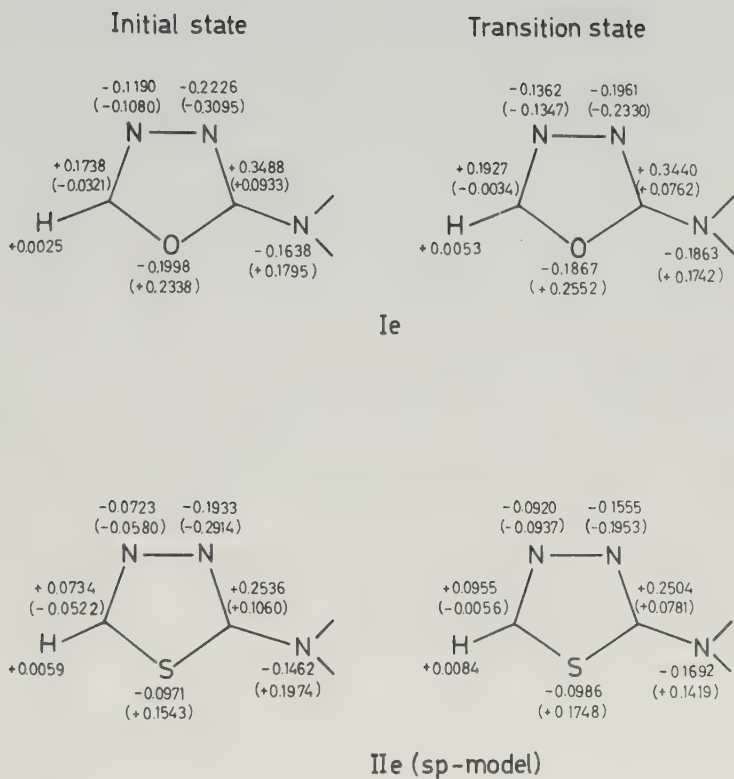


Fig. 30. Total and π -charge densities obtained from CNDO/2 calculations (π -charges are given in parentheses).

The calculations refer to the "planar" dimethylamino group model. The heterocyclic ring plane describes the xy plane and the π -charges have thus been calculated from the electron densities of the p_z -orbitals. (In the spd model the π -charge on sulphur also includes contributions from the d_{xz} - and d_{yz} -orbitals.)

The initial and transition states of the rotation in the 5-unsubstituted compounds Ie and IIe are characterized by a combined σ -electron withdrawal and π -electron release of the exocyclic amino nitrogen atom. The CNDO/2 and the PPP π -charge densities presented earlier (Fig. 14) show an overall similarity, but it can also be noted that the CNDO/2 total and π -charge densities are not equally affected by the rotation of the dimethylamino group. This indicates that changes in the σ -skeleton may be important in the theoretical treatment of the rotation process for the compounds considered in this work.

The donation of π -electron density from the dimethylamino group to the ring system, on going from the transition state to the initial state, is due to delocalization of the amino nitrogen "lone pair". The degree of delocalization in the different compounds in each of the series I and II, as calculated by the difference of the "lone pair" charge density between the transition state and the initial state, is linearly related to the experimental barriers. The relations are shown in Fig. 31. (The barrier value for Ie is that obtained from the Hammett plot in Fig. 7, that is 6.5 kcal/mol.) The points representing the cyano substituted compounds Ib and IIb can not be included in the linear relationships established by the other compounds and this clearly demonstrates the previously mentioned underestimation of the effect of the cyano substituent on the barrier.

The delocalization of the amino nitrogen "lone pair" into the ring system corresponds to an increase in the π -bond order of the exocyclic carbon-nitrogen bond as shown in Fig. 32. The plots represent the nitrogen "lone pair" delocalization, calculated as above, vs. the increase in the carbon-nitrogen π -bond order on going from the transition state to the initial state (Δp_{CN}).

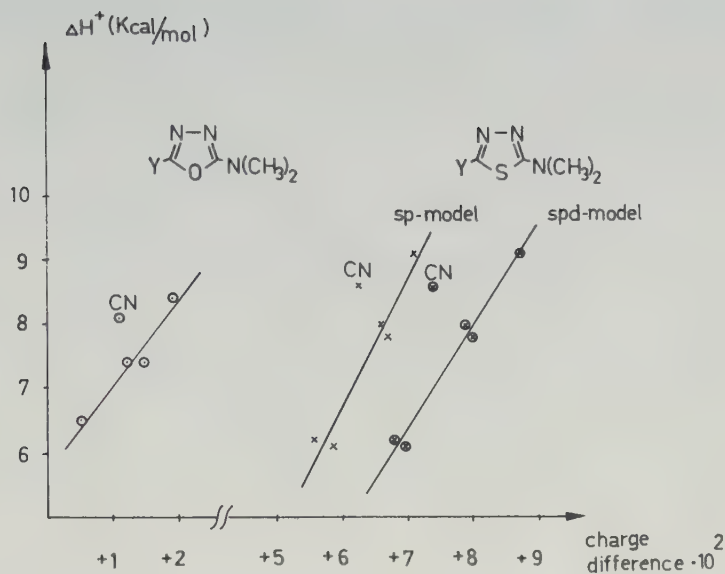


Fig. 31. Difference in "lone pair" charge density (CNDO/2) vs. experimental barriers.

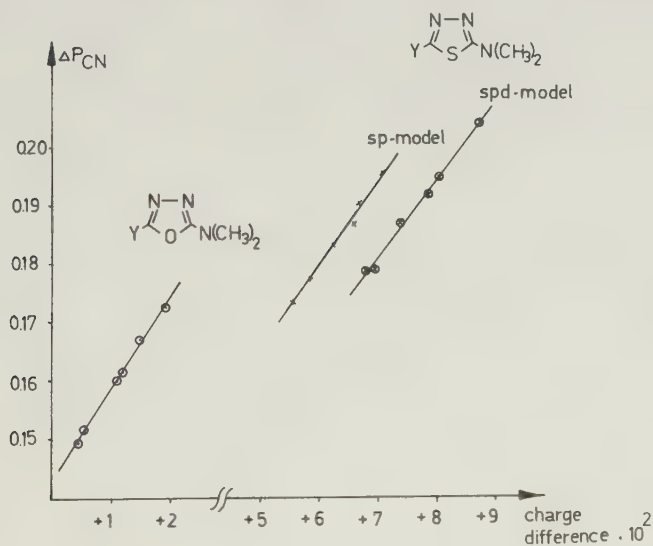


Fig. 32. Difference in "lone pair" charge density (CNDO/2) vs. ΔP_{CN} .

Table 23. Group total and π -charge differences between initial state and transition state.

		Series II		
		Series I	sp-model	spd-model
NO ₂	$\sigma + \pi$	-0.0084	-0.0093	-0.0083
	π	-0.0049	-0.0062	-0.0053
CN	$\sigma + \pi$	-0.0074	-0.0089	-0.0087
	π	-0.0057	-0.0086	-0.0081
CO ₂ Et	$\sigma + \pi$	-0.0091	-0.0102	-0.0115
	π	-0.0067	-0.0087	-0.0089
CF ₃	σ	-0.0069	-0.0062	-0.0073
H	σ	-0.0028	-0.0025	-0.0031
C ₆ H ₅	$\sigma + \pi$	-0.0120	-0.0112	-0.0152
	π	-0.0086	-0.0098	-0.0123

The relations as well as the results from the corresponding PPP calculations support the classical picture of the origin of the barriers to internal rotation in this type of compounds. That is, the delocalization of the amino nitrogen lone pair leads to a partial double bond formation between carbon and nitrogen, which stiffens the bond and hinders rotation around it.

In conformity with the PPP calculations, the substituent effect on the barriers, according to the CNDO/2 calculations, is mainly due to a polarization of the electron distributions in the ring systems. The charge density differences of the substituents between the transition state and the initial state are very small (Table 23) and can not explain the order of the calculated barriers. The main effect of the polarization is in this case, as in the PPP calculations, an increased ability of the amino nitrogen to delocalize its electron "lone pair" over the ring system with increasing electron-withdrawing ability of the substituent.

V. CHEMICAL SHIFTS

The NMR chemical shifts for the dimethylamino protons of compounds Ia-VIb were measured at room temperature using a Varian A-60A spectrometer. The spectra were recorded on 5 % solutions (w/v) in CDCl_3 and the shifts relative to TMS were obtained by the standard side-band technique¹¹⁶. The values are accurate to at least ± 0.1 Hz (0.002 ppm). To get an estimation of the errors introduced by determining the shifts for 5 % solutions instead of evaluating the infinite dilution values, the concentration dependence of the dimethylamino signal was investigated for compound IIe. Fig. 33 shows that the difference between the extrapolated infinite dilution shift and the shift in 5 % solution is very small, ca 0.2 Hz (0.003 ppm). This has been taken as justification for using the values obtained for 5 % solutions.

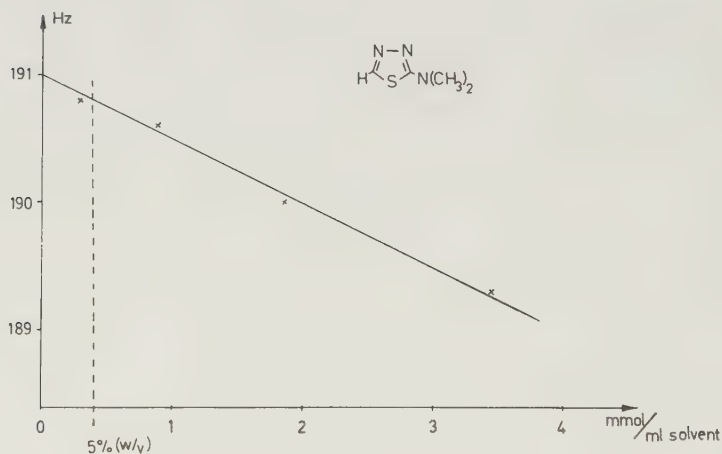


Fig. 33. Concentration dependence of the dimethylamino NMR signal of compound IIe.

Results

The results of the measurements are given in Table 24. The resonance position of the dimethylamino signal of the compounds in series I and II shows a significant dependence on substitution in the 5-position.

Rae and Dyall¹⁷ have observed that the chemical shifts of the N-dimethyl protons in fifteen para-substituted N,N-dimethyl anilines are linearly correlated with the Hammett σ^- -constants with a correlation coefficient of 0.965. They also noted that no meaningful correlation could be found if the "normal" σ_p -constants were used. As shown in Fig. 34 the corresponding chemical shifts of compounds Ia-e and IIa-e can also be fitted to a Hammett plot and even in this case the enhanced σ^- -values are necessary. The correlation coefficients are 0.986 and 0.997 for series I and II respectively, and the slopes of the lines are 9.00 and 9.64, quite close to the value 10.10, found by Rae and Dyall. (The phenyl and methyl substituted compounds could not be fitted to the straight lines in Fig. 34. The relations found for series I and II thus only include compounds with electron-withdrawing substituents.)

The parallelism found between series I and II and the N,N-dimethylanilines is not unexpected in view of the similar results obtained earlier for the substituent effect on the rotational barrier of the dimethylamino group. In that connection it was shown that the barriers in series I and II paralleled the degree of amino nitrogen "lone pair" delocalization as measured by changes in π -electron density on the nitrogen atom. The charge on the exocyclic nitrogen atom can be expected to influence the methyl proton shift in conformity with the observation that chemical shifts in methyl esters can be correlated with the electron density at the oxygen atom adjacent to the methyl group¹¹⁷. It has also been observed that the electronegativity of the halide atom in methyl halides influences the proton shifts in these compounds¹¹⁸.

Table 24. Dimethylamino proton shifts in CDCl_3 relative to TMS.

Compound	Shift (Hz)	Shift (δ ppm)
Ia	194.6	3.24
Ib	192.0	3.20
Ic	191.4	3.19
Id	190.2	3.17
Ie	186.7	3.12
If	188.0	3.13
Ig	183.3	3.06
IIa	197.8	3.30
IIb	196.6	3.28
IIc	194.7	3.25
IId	193.6	3.23
IIe	190.8	3.18
IIIf	192.5	3.21
IIg	186.3	3.11
III	190.0	3.17
IV	198.0	3.30
Va	178.8	2.98
Vb	176.6	2.94
Vc	173.4	2.89
Vd	183.0	3.05
Ve	172.5	2.88
VIa	183.0	3.05
VIb	182.8	3.05

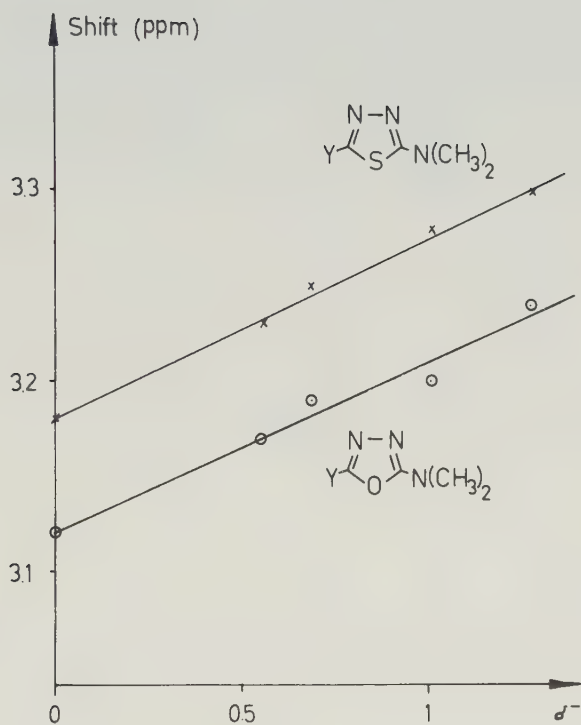


Fig. 34. Hammett correlations for compounds Ia-e and IIa-e.

To study the relationship between chemical shift and electron densities, the shielding constant σ_A for a nucleus A may be written as a sum of atomic and inter-atomic contributions¹¹⁹.

$$\sigma_A = \sigma_d^{AA} + \sigma_p^{AA} + \sum_{B \neq A} \sigma_{AB} + \sigma_{A, \text{ring}} \quad (25)$$

where σ_d^{AA} and σ_p^{AA} are the diamagnetic and paramagnetic contributions respectively from the electrons of atom A. σ_{AB} is the contribution from electrons on atom B and $\sigma_{A, \text{ring}}$ is a term due to nonlocalized ring currents. The chemical shift δ_{AB} between protons A and B is given by

$$\delta_{AB} = \sigma_A - \sigma_B \quad (26)$$

The term σ_p^{AA} is considered to be less important for protons¹¹⁸. The contribution σ_a^{AA} can be estimated as

$$\sigma_d^{AA} = \frac{e^2}{3 mc^2} \int \frac{\lambda \psi_{1s}^2}{r} d\tau = 21.4 \lambda \cdot 10^{-6} \quad (27)$$

where λ represents the effective number of electrons in the hydrogen 1s-orbital (ψ_{1s})¹¹⁸.

Equations (25) and (27) indicate that if the second term in (25) can be neglected and if the two last terms are constant in a series of compounds, the hydrogen electron density should correlate with the chemical shift. Such a correlation has been found in an all-valence-electron treatment of aliphatic compounds¹²⁰. In compounds Ia-f and IIa-f no correlation could, however, be found between hydrogen charge densities, as calculated by the CNDO/2 method, and the chemical shifts.

Table 25. Average hydrogen formal charges. Values calculated by the spd model are within parentheses.

Compound	Hydrogen charge	
Ia	+ 0.0055	
Ib	+ 0.0009	
Ic	+ 0.0008	
Id	+ 0.0023	
Ie	- 0.0001	
If	- 0.0015	
IIa	+ 0.0053	(+ 0.0062)
IIb	+ 0.0008	(+ 0.0021)
IIc	+ 0.0010	(+ 0.0022)
IId	+ 0.0023	(+ 0.0036)
IIe	- 0.0001	(- 0.0002)
IIf	- 0.0021	(- 0.0001)

Table 25 gives the calculated hydrogen charges (averaged over the six protons in the dimethylamino group). The substituent effect on the hydrogen charges is seen to be very small. Since the electron density around the hydrogen nucleus is also small compared to that in heavier atoms, contributions to the chemical shift from other atoms (and bonds) in the molecule is expected to be important. Assuming that the ring current effect $\sigma_{A,ring}$ varies very little within each series of compounds (I and II) and considering that the magnetic anisotropies from other atoms fall off as $\frac{1}{R^3}$ ¹²¹, it may be suspected that variations of the nearby nitrogen charge have a strong influence on the chemical shift of the dimethylamino signal. Attempts to

correlate the chemical shift with the total charge density on the exocyclic nitrogen atom were unsuccessful, but a fair correlation between the nitrogen "lone pair" charges ($q_N(\pi)$) calculated by the CNDO/2 method and the chemical shifts could be obtained. Fig. 35 shows this relationship for the compounds in series I and II. The points in parentheses represent the cyano substituted compounds. These have been neglected since, as demonstrated earlier in this work, the electronic effects of this substituent are not appropriately treated by the CNDO/2 approximation. The correlation coefficient is 0.94 for all three plots.

Further support for the dominating influence of the changes of the nitrogen "lone pair" charge on the proton chemical shifts of the dimethylamino group is found by π -electron calculations. Fig. 36 shows plots of nitrogen "lone pair" charges calculated by the PPP method, using parametrization scheme A described earlier, vs. the chemical shifts. The correlations obtained show that the variation of the amino nitrogen "lone pair" charge densities can satisfactorily account for changes of the dimethylamino proton chemical shifts caused by substitution in the 5-position of compounds in series I and II. Ring aza substitution of compound IIe, which gives compound IV, shifts the dimethylamino signal to lower field by 0.12 ppm (Table 24). This displacement is qualitatively predicted by the formal nitrogen charges which are + 0.0516 and + 0.0533 respectively, but the values for compound IV can not be fitted to the linear relation shown in Fig. 36 indicating that ring aza substitution gives significant changes in the anisotropy and/or ring current terms in equation (25). Ring aza substitution of compound III leads to a similar downfield displacement, 0.13 ppm, but this time the PPP calculations are not able to predict the direction of the displacement. This failure is also noted in the analogous compounds Vc and VIb where the exocyclic nitrogen charges are + 0.0579 and + 0.0562 respectively, predicting an upfield shift of the dimethylamino signal upon aza substitution in Vc. Experimentally, a downfield shift of 0.16

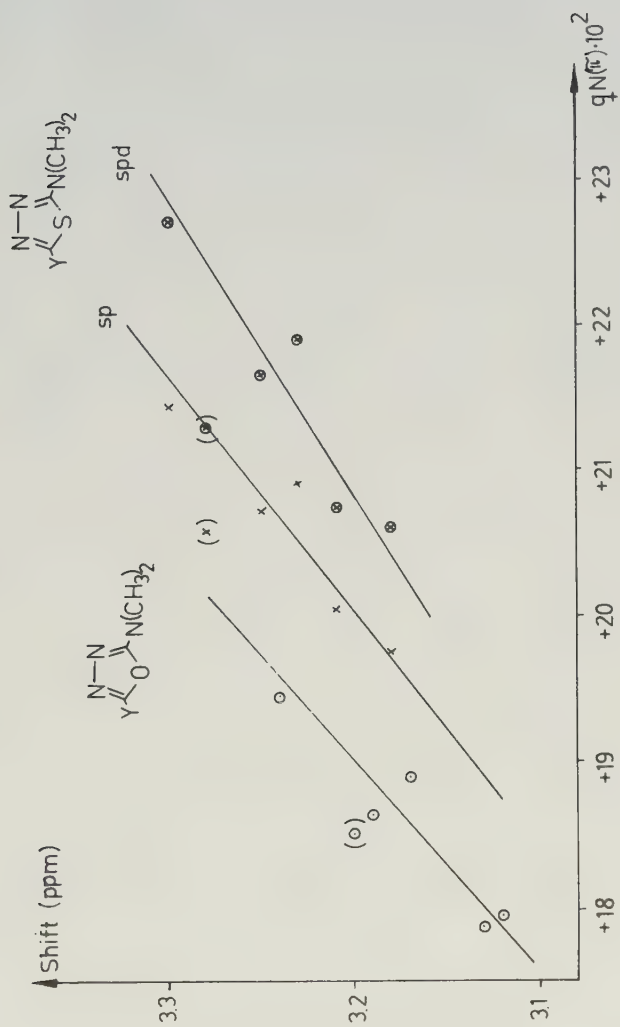


Fig. 35. "Lone pair" charge density (CNDO/2) vs. dimethylamino chemical shift.

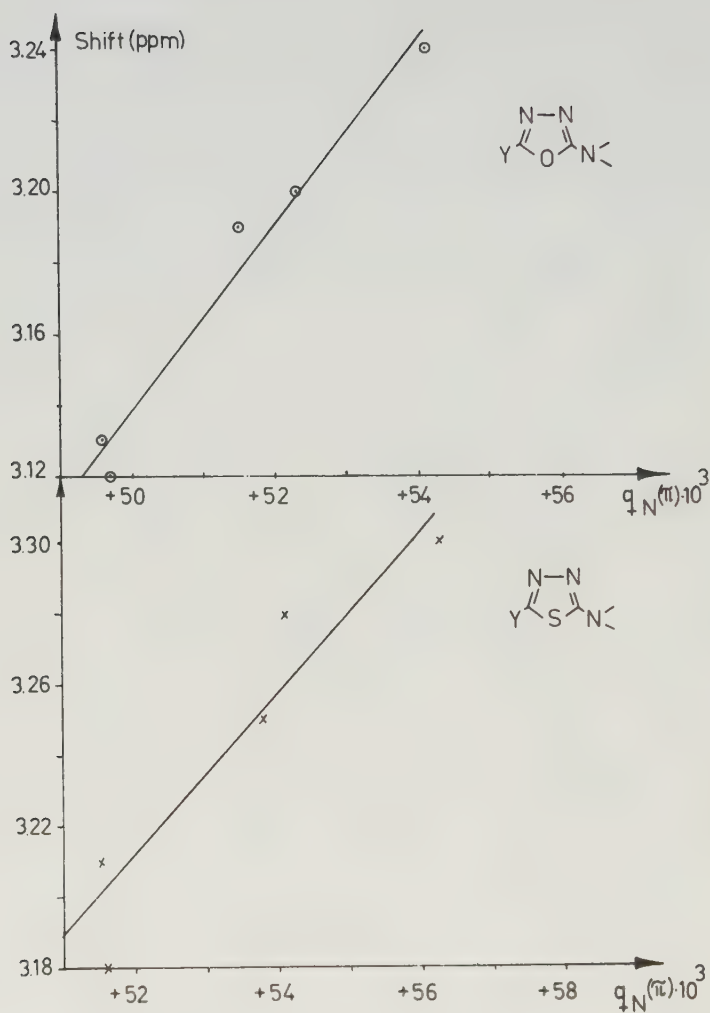


Fig. 36. "Lone pair" charge density (PPP) vs. dimethylamino chemical shift.

ppm is found. In the pair of compounds Va and VIa, however, the effect of the ring aza substituent is correctly predicted. The nitrogen charges are here + 0.0507 and + 0.0513 respectively. This shows that prediction of chemical shifts made on the basis of electron densities must be made with caution and must generally be restricted to closely related compounds.

VI. ULTRAVIOLET SPECTRA

Ultraviolet spectra of the compounds considered in this work have been studied and compared to theoretical values obtained from PPP calculations. The spectra were recorded on a Unicam Model Sp 800 spectrophotometer. A mixture of cyclohexane and methylene chloride (3 % v/v) was used as solvent. (It was necessary to add a small amount of methylene chloride to allow all compounds to be studied in the same solvent.)

The PPP calculations were performed using the two parametrization schemes described in chapter IV and denoted A and B. Within scheme B the calculations were divided into two sets, B and B'. In scheme B', methyl groups were included in the calculations. Interaction between singly excited configurations have been included in the calculations. In calculations using scheme A a maximum of 20 configurations were mixed, while in scheme B calculations, all singly excited configurations were included in the configuration interaction.

Experimental and calculated absorption wavelengths and intensities are given in Table 26.

In comparisons between experimental and theoretical values it should be noted that most of the parameters used in the PPP calculations have been calibrated using vapor phase spectra while the experimental spectra refer to compounds in solution. Very little is known about the difference between vapor phase and solution spectra of compounds similar to those under consideration. 1,3-Thiazole has an absorption maximum at 228 nm in the gas phase⁷⁷, while the corresponding value in ethanol is 240 nm¹²², a bathochromic shift of 12 nm. Bathochromic shifts of 10-20 nm on going from the gas phase to solution have been observed for thiophenes¹²³. Large solvent shifts in substituted benzenes are observed primarily when the substituent is an electron acceptor. Donor substituents cause much smaller shifts. In aniline the solvent shifts are 3-5 nm (hydrocarbon solvents) depending on the band considered^{124,125}.

Table 26. Experimental and calculated ultraviolet spectra.

Comp.	Calculated values							
	Experimental		Scheme A		Scheme B		Scheme B'	
	$\lambda_{\max}$ (nm)	ϵ	wave length (nm)	f	wave length (nm)	f	wave length (nm)	f
Ia	343	10400	270	0.065	332	0.436	336	0.435
	220	6100	203	0.030	231	0.006	231	0.003
Ib	291 sh	8000	230	0.342	271	0.637	274	0.631
	279	11900	186	0.110	206	0.002	206	0.001
Ic	298 sh	5300	224	0.231	272	0.555	274	0.553
	286	8300	182	0.060	205	0.006	205	0.005
Id	245	7900						
Ie	233	6300	194	0.177	240	0.396	243	0.397
If	309 sh	8900	266	0.003	281	0.813	283	0.811
	292	15900	238	0.443	270	0.032	270	0.027
	223	9200	200	0.149	210	0.033	211	0.032
Ig	229	6400					243	0.410
IIa	361	8900	274	0.078	323	0.578	329	0.580
	230	3900	238	0.013	226	0.072	228	0.070
IIb	309	15100	240	0.415	280	0.804	285	0.791
	224	3700	208	0.090	227	0.042	228	0.038
IIc	312	11900	233	0.295	280	0.706	285	0.699
	225	4000	204	0.066	218	0.021	219	0.017
IId	282	9400						
	220	3900						
IIe	267	6400	202	0.236	255	0.537	259	0.531
	225	1600	192	0.043	221	0.064	221	0.064
IIIf	334 sh	8600	267	0.004	293	1.022	297	1.009
	313	17200	246	0.519	269	0.011	270	0.009
	228	7600	202	0.109	225	0.007	225	0.004

Table 26. (continued)

Comp.	Calculated values							
	Experimental		Scheme A		Scheme B		Scheme B'	
	$\lambda_{\max}$ (nm)	ϵ	wave length (nm)	f	wave length (nm)	f	wave length (nm)	f
IIg	265	7700					260	0.551
	221	3000					215	0.041
III	256	10000	208	0.196				
	221	3000	189	0.165				
IV	274	6900	213	0.189				
	259 sh	4700	201	0.092				
	220	3100	169	0.321				
Va	242	3400	210	0.111	224	0.178		
	224	3000	184	0.106	194	0.240		
Vb	240	4300						
	217	6400						
Vc	224	4200	203	0.252	202	0.378		
Vd	292 br	2100	254	0.016	340	0.218		
	225	12900	212	0.080	245	0.067		
Ve	224	3500	198	0.191	225	0.422		
VIa	266	3700	237	0.118	221	0.208		
	217	5700	195	0.173	190	0.108		
VIb	228	6900	225	0.159	209	0.306		
	218	9700	196	0.058	189	0.026		

sh = shoulder, br = broad

The spectra of nitro substituted benzenes show larger shifts, 13-14 nm¹²⁶. In all cases bathochromic shifts are observed. Another factor which must be considered is the shift produced by methyl substitution of an amino group, since using schemes A and B the calculations refer to amino rather than to dimethylamino substituted compounds. It has been shown that N-methylation may give significant shifts in the UV spectrum. N,N-Dimethylaniline shows a bathochromic shift of 17 nm relative to aniline in hydrocarbon solvents¹²⁷, compound IV absorbs at 12-15 nm¹²⁷ and compound VIb at 15 nm longer wavelength than the corresponding amino compounds⁴⁴. Scheme B' has been used in an attempt to account for such shifts. In Table 26 is seen that inclusion of N-methyl groups gives calculated bathochromic shifts of 2-6 nm for the long-wavelength band while the other bands are almost unaffected. Considering the data presented above, the calculations probably somewhat underestimate the effect of N-methyl groups on the UV transitions. It seems reasonable, taking the solvent effect and the N-methyl shift into account, to expect the calculated values to be 15-30 nm lower than the experimental ones in calculations using schemes A and B. An examination of Table 26 shows that scheme B (and B') gives the most realistic values for the transition energies. The overall agreement between calculated (schemes B and B') and experimental values, taking the estimated corrections into account, is in most cases good. Scheme A gives transition energies which are certainly too high.

The unsubstituted 1,3,4-oxadiazole and 1,3,4-thiadiazole have no absorption maxima above 200 and 220 nm, respectively^{30,129}. Substitution by a dimethylamino group, with its ability to interact with the π -system of the ring, produces large bathochromic shifts in the UV spectrum. The reason for the too short wavelengths calculated by scheme A can at least partly be found in the way this parametrization scheme treats the interaction between the dimethylamino group and the heterocyclic ring system. The calculated bathochromic

shifts due to dimethylamino substitution in 1,3,4-oxadiazole and 1,3,4-thiadiazole are only 13 and 9 nm, respectively, when scheme A is used. These values are too low by at least 20 and 40 nm, respectively. The corresponding values calculated by scheme B are 27 and 23 nm, respectively. These values are probably also somewhat too low but the use of scheme B results in a significant improvement. The better agreement between experiment and calculation according to scheme B is certainly due to the allowance made for neighbouring atom influence on the parameters in this scheme (see chapter IV).

The long wavelength bands at 233 nm in Ie and at 267 in IIe are strongly affected by substitution. The ability of the electron-withdrawing substituents to displace this band to longer wavelengths is in the order $\text{NO}_2 > \text{CO}_2\text{C}_2\text{H}_5 > \text{CN} > \text{CF}_3$ in both series. This is the same order as that observed for the corresponding para-substituted anilines^{18,19,130,131}, again demonstrating the similarities of substituent effects on properties of anilines, dimethylamino-1,3,4-oxa- and thiadiazoles. However, this resemblance seems to be restricted to electron-withdrawing substituents. We have previously seen that the methyl substituent could not be fitted into this scheme (chapter V, Fig. 34). This is also observed when ultraviolet spectra are studied. A methyl group in the para position of aniline produces a red shift in the UV spectrum¹²⁷, while a methyl substituent in the 5-position of compounds Ie and IIe results in a small blue shift of all transitions. This is also the case for the triazole compound Va.

Compounds If and IIf which have a phenyl group in the 5-position, show two close lying absorption maxima with a separation of about 20 nm. Najer *et al.*²⁶ report only one maximum in this region in the spectrum of compound IIf in ethanol ($\lambda_{\text{max}} = 290 \text{ nm}$, $\epsilon = 16800$). Similarly, only one maximum is obtained for 2-amino-5-phenyl-1,3,4-thiadiazole and the corresponding 2-diethylamino compound in water ($\lambda_{\text{max}} = 295$, $\epsilon = 14000$ and $\lambda_{\text{max}} = 320$, $\epsilon = 17300$, respectively)¹³². The PPP calculations (Table 26) support the existence of two

separate and close lying transitions. The spectra of compounds Ib and Ic also show two maxima, this time separated by 12 nm. In this case, however, calculations only predict one transition in this region for each of the compounds. The shape of the long wavelength bands in the spectra of these compounds may therefore be due to vibrational fine structure. The ability of the PPP method to reproduce substituent effects can be studied by comparing experimental and calculated shifts relative to the 5-unsubstituted compounds Ie and IIe. The results are shown in Table 27.

Table 27. Absorption maxima (nm) relative to Ie and IIe.

Compound	Exp.	Scheme A	Scheme B	Scheme B'
Ia	110	76	92	93
Ib	58,46	36	31	31
Ic	65,53	30	32	31
Ie	0	0	0	0
If	76,59	72,44	41,30	40,27
Ig	-4	-	-	0
IIa	94	72	68	70
IIb	42	38	25	26
IIc	45	31	25	26
IIe	0	0	0	0
IIIf	67,46	65,44	38,14	38,11
IIg	-2	-	-	1

All three schemes give a qualitatively correct picture of the substituent effects on the UV transitions in series I and II. Numerically the calculated values are consistently too low (except for Ig and IIg). Part of the discrepancies may be due to differences in solvent shifts for the 5-unsubstituted compounds and the compounds with electron-withdrawing substituents, in analogy with the smaller solvent shift found for aniline than for nitrobenzene. Most of the differences between experiment and calculation, however, probably reflect the limitations of the π -electron approximation.

Compound III absorbs at shorter wavelength than the isomeric compound IIe, contrary to what is predicted by the calculations. Aza substitution in IIe and III gives in both cases red shifts in the UV spectra. This is opposite to what is found for benzene and its aza derivatives, where aza substitution generally shifts the first π - π^* band to shorter wavelength¹³³. The PPP calculations successfully predict the directions of shifts due to aza substitution in the present case.

1,2,4-Triazole and its alkyl derivatives have no absorption above 215 nm (ethanol)¹³⁴ and tetrazoles without conjugating substituents show only end absorption¹³⁵. From Table 26 it is clear that also in these compounds dimethylamino substitution results in significant bathochromic shifts. A comparison between experimental and calculated spectra is not straightforward in these cases, since some of the compounds for steric reasons probably have twisted dimethylamino groups, which is not taken into account in the calculations. Ortho methyl substituted N,N-dimethylaniline, however, only shows a small shift (3 nm) due to the ortho methyl group so it may be assumed that the steric effects of the ring N-methyl groups on the UV spectra of 1,2,4-triazoles Va-e and tetrazoles VIa-b are also small. In the 1,2,4-triazole series the long wavelength band is displaced to longer wavelengths in the order $V_e = V_c < V_a$, and in the tetrazole series the order is $VI_b < VI_a$. These displacements are satisfactorily reproduced by the calculations, except that the value calculated for compound Ve is too high when scheme B is used. In conformity with the observations made

in the oxa- and thiadiazole series, aza substitution in 1,2,4-triazoles produces a red shift of the long wavelength band in these compounds. Calculations using scheme A predict red shifts in all cases, while calculations according to scheme B are less successful, predicting blue shifts for aza substitution in compounds Va and Ve. In the latter case, this is probably due to the too low transition energy calculated for Ve, as mentioned above.

VII. PREPARATIVE PART

The syntheses are given according to the numbering of the compounds (I-VI), which means that in some cases the synthesis of the starting material is described after the synthesis of the end product.

1,3,4-Oxadiazoles

2-Dimethylamino-5-nitro-1,3,4-oxadiazole (Ia). 1.13 g (0.010 mol) of 2-dimethylamino-1,3,4-oxadiazole (Ie) was added dropwise with stirring and cooling (0-5°C) to a mixture of sulphuric acid (3 ml) and fuming nitric acid (0.5 ml). The resulting mixture was kept at 0-5°C over night and then poured onto ice. Extraction of the water solution with chloroform and evaporation of the chloroform layer gave 0.43 g (27 %) of the desired product, m.p. 82-83.5°C after recrystallization from toluene/ligroin. Calcd. for $C_4H_6N_4O_3$ (158.12): C 30.4; H 3.83; N 35.4. Found: C 30.8; H 3.93; N 35.1.

2-Dimethylamino-5-carbamoyl-1,3,4-oxadiazole. 12 g (0.065 mol) of 2-dimethylamino-5-ethoxycarbonyl-1,3,4-oxadiazole (Ic) was dissolved in abs. ethanol (250 ml). After cooling to 0°C a stream of ammonia was passed through the solution, which was then kept at 0°C for another three hours and at room temperature over night. The product precipitated spontaneously. Yield: 8.2 g (81 %); m.p. 192.5-193°C after recrystallization from abs. ethanol. Calcd. for $C_5H_8N_4O_2$ (156.15): C 38.5; H 5.16; N 35.9. Found: C 38.3; H 5.48; N 35.4.

2-Dimethylamino-5-cyano-1,3,4-oxadiazole (Ib). 7.75 ml of titanium tetrachloride in carbon tetrachloride (20 ml) was added dropwise with stirring and cooling (0-5°C) to 150 ml of dry tetrahydrofuran (THF). 6.0 g (0.038 mol) of 2-dimethylamino-5-carbamoyl-1,3,4-oxadiazole was then added in portions. Finally 20.2 ml of triethylamine in dry THF (25 ml) was added dropwise during one hour and the resulting mixture was stirred

for another six hours. After addition of 50 ml of water, the water solution was extracted with chloroform, the chloroform layer was evaporated and the solid residue was extracted with several portions of boiling petroleum ether (40-60°C). The product precipitated from this solution after cooling, yielding 3.5 g (67 %), m.p. 45.5-46.5°C after recrystallization from petroleum ether. Calcd. for $C_5H_6N_4O$ (138.13): C 43.5; H 4.38; N 40.6. Found: C 43.7; H 4.80; N 39.8.

Ethyl glyoxalate 4,4-dimethylsemicarbazone was prepared from 7.1 g (0.069 mol) of 4,4-dimethylsemicarbazide¹³⁶ and 7.1 g (0.069 mol) of ethyl glyoxalate²⁸ in ethanol (50 ml). After twelve hrs, 9.3 g (71 %) of the desired semicarbazone had separated from the solution; m.p. 158-159.5°C after recrystallization from toluene or methanol. Calcd. for $C_7H_3N_3O_3$ (187.20): C 44.9; H 7.00; N 22.5. Found: C 44.2; H 7.25; N 22.2.

2-Dimethylamino-5-ethoxycarbonyl-1,3,4-oxadiazole (Ic). To a suspension of 4 g (0.021 mol) of ethyl glyoxalate 4,4-dimethylsemicarbazone and 7.04 g of anhydrous sodium acetate in acetic acid (20 ml), 1.7 ml (0.021 mol) of bromine was added dropwise during two hrs. The temperature was kept below + 40°C. The reaction mixture was stirred for 45 minutes, 40 ml of water was added and the water solution was extracted with chloroform. Evaporation of the chloroform layer gave a solid residue (the hydrobromide of Ic) which was dissolved in water and neutralized with $KHCO_3$. Extraction with chloroform and evaporation of the chloroform solution yielded 1.9 g (49 %) of Ic, m.p. 45-46°C after recrystallization from ligroin. Calcd. for $C_7H_{11}N_3O_3$ (185.18): C 45.4; H 5.99; N 22.7. Found: C 45.4; H 6.06; N 22.8.

1-Trifluoroacetyl-4,4-dimethylsemicarbazide 12 g (0.12 mol) of 4,4-dimethylsemicarbazide was mixed with 30 ml of trifluoroacetic anhydride at -5 - 0°C. The reaction mixture was then stirred at room temperature for one hr. After the addition of water (25 ml), the product precipitated and 15.1 g (63 %) could be collected. Recrystallization from water gave m.p. 184.5-186.0°C. Calcd. for $C_5H_8F_3N_3O_2$ (199.13): C 30.2; H 4.05; N 21.1. Found: C 30.4; H 4.46; N 20.7.

2-Dimethylamino-5-trifluoromethyl-1,3,4-oxadiazole (Id). A mixture of 8 g (0.040 mol) of 1-trifluoroacetyl-4,4-dimethylsemicarbazide and 60 ml of phosphorous oxychloride was refluxed for one hr. After cooling to room temperature, the reaction mixture was added dropwise to ice/water with stirring. The resulting water solution was made alkaline with NaOH and left at + 5°C over night. Precipitated salts were removed by filtration and washed with chloroform. The water solution was extracted with chloroform and the combined chloroform solutions were evaporated to yield a yellow oil, which was distilled and the desired product was collected at 47-48°C (1.2 mm). Yield: 2.9 g (40 %). Calcd. for $C_5H_6F_3N_3O$ (181.11): C 33.2; H 3.34; N 23.2. Found: C 33.9; H 4.01; N 23.0.

1-Formyl-4,4-dimethylsemicarbazide was prepared by heating a mixture of 10.3 g (0.10 mol) of 4,4-dimethylsemicarbazide and 13.8 g of formic acid at 110°C for half an hour. Removal of the excess of formic acid gave 12.3 g (94 %) of the crude product, which was recrystallized from toluene-ethanol; m.p. 151-152°C. Calcd. for $C_4H_9N_3O_2$ (131.14): C 36.6; H 6.92; N 32.0. Found: C 37.0; H 7.08; N 31.7.

2-Dimethylamino-1,3,4-oxadiazole (Ie) was prepared by the same procedure as that described for the synthesis of compound Id, from 10 g (0.076 mol) of 1-formyl-4,4-dimethylsemicarbazide and 75 ml of phosphorous oxychloride. 5.5 g (64 %) of the desired product was collected at 73-74°C (1.5 mm). Calcd. for $C_4H_7N_3O$ (113.12): C 42.5; H 6.24; N 37.2. Found: C 42.2; H 6.66; N 36.5.

1-Benzylidene-4,4-dimethylsemicarbazide. 10.3 g (0.01 mol) of 4,4-dimethylsemicarbazide was mixed with 10.6 g (0.01 mol) of benzaldehyde in ethanol. The product precipitated immediately. 15.3 g (80 %) of 1-benzylidene-4,4-dimethylsemicarbazide was obtained with m.p. 191-192°C after recrystallization from ethanol. (Lit.¹³⁶ m.p. 192°C.)

2-Dimethylamino-5-phenyl-1,3,4-oxadiazole (If). This compound was prepared according to Najer et al.²⁶, m.p. 83-83.5°C. (Lit. m.p. 84-85°C.)

1-Acetyl-4,4-dimethylsemicarbazide. 10.3 g (0.1 mol) of 4,4-dimethylsemicarbazide was mixed with 30 ml acetic acid anhydride. The product soon started to precipitate, and after two hrs 6.8 g (61 %) could be collected. Recrystallization from chloroform-petroleum ether gave m.p. 158-159.5°C. Calcd. for $C_5H_{11}N_3O_2$ (145.16): C 41.4; H 7.64; N 29.0. Found: C 41.4; H 7.66; N 28.5.

2-Dimethylamino-5-methyl-1,3,4-oxadiazole (Ig) was prepared by the same method as compounds Id and Ie, from 4.0 g (0.028 mol) of 1-acetyl-4,4-dimethylsemicarbazide and 50 ml of phosphorous oxychloride. Yield: 2.6 g (72 %) boiling at 69°C (1.2 mm). Calcd. for $C_5H_9N_3O$ (127.15): C 47.2; H 7.14; N 33.1. Found: C 46.9; H 7.19; N 32.6.

1,3,4-Thiadiazoles

2-Dimethylamino-5-nitro-1,3,4-thiadiazole (IIa). 1.3 g (0.01 mol) of 2-dimethylamino-1,3,4-thiadiazole (IIe) was dissolved in 3 ml of conc. sulphuric acid. 3 ml of fuming nitric acid was added and the mixture was heated on a water bath for 30 min. After cooling to room temperature the reaction mixture was poured onto ice-water. 1.1 g (65 %) of IIa precipitated. Recrystallization from ethanol gave m.p. 140-141°C. Calcd. for $C_4H_6N_4O_2S$ (174.18): C 27.5; H 3.35; N 32.3; S 18.2. Found: C 27.6; H 3.47; N 32.2; S 18.4.

2-Dimethylamino-5-carbamoyl-1,3,4-thiadiazole was prepared by shaking 2.5 g (0.12 mol) of 2-dimethylamino-5-ethoxycarbonyl-1,3,4-thiadiazole (IIc) with an excess of conc. ammonia for half an hour. The product separated, and 2.0 g (93 %) was collected, m.p. 224.5-225.5°C after recrystallizing from water. Calcd. for $C_5H_8N_4OS$ (172.21): C 34.9; H 4.68; N 32.5; S 18.6. Found: C 35.0; H 4.73; N 32.4; S 18.7.

2-Dimethylamino-5-cyano-1,3,4-thiadiazole (IIb) was prepared by the same procedure as that described for Ib, from 1.25 g (0.073 mol) of 2-dimethylamino-5-carbamoyl-1,3,4-thiadiazole, yielding

0.71 g (63 %) of the desired product, m.p. 57-57.5°C after recrystallization from petroleum ether (40-60°C). Calcd. for $C_5H_6N_4S$ (154.20): C 38.9; H 3.92; N 36.3; S 20.8. Found: C 39.2; H 4.21; N 36.3; S 20.9.

Ethyl glyoxalate 4,4-dimethylthiosemicarbazone was prepared by mixing 11.9 g (0.10 mol) of 4,4-dimethylthiosemicarbazide¹³⁷ and 10.2 g (0.10 mol) of ethyl glyoxalate in 50 ml of warm ethanol. After 24 hrs at room temperature, 12.7 g (63 %) of the thiosemicarbazone had precipitated; m.p. 131.5-132.5°C after recrystallization from ethanol. Calcd. for $C_7H_{13}N_3O_2S$ (203.26): C 41.4; H 6.45; N 20.7; S 15.8. Found: C 41.5; H 6.10; N 20.7; S 15.8.

2-Dimethylamino-5-ethoxycarbonyl-1,3,4-thiadiazole (IIc). 4.2 g (0.02 mol) of ethyl glyoxalate 4,4-dimethylthiosemicarbazone was dissolved in 50 ml of acetic acid and 8 g of ferric chloride hexahydrate in 25 ml of water was added with stirring. The reaction mixture was left at room temperature for 20 hrs and then extracted with ether. Evaporation of the ether solution gave 1.7 g (43 %) of crude product, m.p. 70-71°C after recrystallization from ligroin. Calcd. for $C_7H_{11}N_3O_2S$ (201.25): C 41.8; H 5.51; N 20.9; S 15.9. Found: C 41.0; H 5.29; N 20.9; S 16.0.

2-Dimethylamino-5-trifluoromethyl-1,3,4-thiadiazole (IIId) was prepared according to the procedure described by Lalezari and Shargi¹³⁸ from 5.3 g 4,4-dimethylthiosemicarbazide trifluoroacetic anhydride, yielding 5.0 g (57 %), m.p. 50.5-52°C after recrystallization from petroleum ether (40-60°C). Calcd. for $C_5H_6F_3N_3S$ (197.18): C 30.5; H 3.07; N 21.3; S 16.3. Found: C 30.9; H 3.63; N 21.5; S 16.2.

1-Formyl-4,4-dimethylthiosemicarbazide. 13.1 g (0.11 mol) of 4,4-dimethylthiosemicarbazide and 40 ml of 80 % formic acid was heated at 130°C on an oil bath for half an hour. After cooling to room temperature, the excess of formic acid was removed. The oily residue crystallized after cooling, giving 10.6 g (66 %) of the desired product, m.p. 131.5-133°C after

recrystallization from ethanol. Calcd. for $C_4H_9N_3OS$ (147.20): C 32.6; H 6.16; N 28.5; S 21.8. Found: C 32.5; H 6.24; N 28.6; S 21.8.

2-Dimethylamino-1,3,4-thiadiazole (IIe). 7.35 g (0.050 mol) of 1-formyl-4,4-dimethylthiosemicarbazide was suspended in chloroform, and an excess of acetyl chloride was added. The reaction mixture became warm and was left with stirring until it had returned to room temperature. It was then refluxed for one hr. After removal of the solvent and the excess of acetyl chloride, the residue was dissolved in the minimum amount of water and the solution was made alkaline with conc. NaOH. Extraction with chloroform and evaporation of the chloroform layer gave an oily residue which was distilled in vacuum. 3.4 g (53 %) of 2-dimethylamino-1,3,4-thiadiazole was obtained at 78-80°C (0.2 mm). [Lit.¹³⁹ b.p. 93-94°C (0.4 mm)]. Calcd. for $C_4H_7N_3S$ (129.18): C 37.2; H 5.46; N 32.5; S 24.8. Found: C 37.1; H 5.83; N 31.8; S 24.6.

1-Benzylidene-4,4-dimethylthiosemicarbazide was prepared by mixing 5.95 g (0.05 mol) of 4,4-dimethylthiosemicarbazide and 5.3 g (0.05 mol) of benzaldehyde in 50 ml of ethanol. The product precipitated, and 10.2 g (98 %) could be collected after one hr. Recrystallization from ethanol gave m.p. 150.5-152°C. Calcd. for $C_{10}H_{13}N_3S$ (207.30): C 57.9; H 6.32; N 20.3; S 15.5. Found: C 57.4; H 6.07; N 20.8; S 15.7.

2-Dimethylamino-5-phenyl-1,3,4-thiadiazole (IIf). 6.2 g (0.030 mol) 1-benzylidene-4,4-dimethylthiosemicarbazide was suspended in 200 ml of water. The suspension was heated to 85°C and 24.3 g of ferric chloride hexahydrate was added in one portion. Half an hour later the mixture was filtered warm. After cooling the hydrochloride of IIf separated; it was collected and dissolved in 2.5 M NaOH and heated on a water bath for half an hour. The desired product precipitated from this solution after cooling. A yield of 3.0 g (40 %) was obtained, m.p. 97-98°C after recrystallization from petroleum ether-benzene or petroleum ether-chloroform. (Lit.²⁹ m.p. 98°C.)

2-Dimethylamino-5-methyl-1,3,4-thiadiazole (IIg). 11.9 g (0.10 mol) 4,4-dimethylthiosemicarbazide was mixed with 30.6 g (0.30 mol) of acetic acid anhydride. After one hr, an excess of acetyl chloride was added to the resulting crystalline mass. After stirring the mixture for one hr, the solution was evaporated. The oily residue was dissolved in water and the water solution was made alkaline with 2.5 M NaOH. Extraction several times with ether and evaporation of the ether layer gave a yellow oil which was distilled in vacuum. The fraction boiling at 86-87°C (0.8 mm) was collected. Yield: 6.2 g (43 %). Calcd. for $C_5H_9N_3S$ (143.21): C 41.9; H 6.34; N 29.3; S 22.4. Found: C 41.9; H 6.71; N 28.7; S 22.7.

5-Dimethylamino-1,2,4-thiadiazole (III) was prepared from 5-chloro-1,2,4-thiadiazole³⁵ and dimethylamine in ethanol as described by Goerdeler³⁴; m.p. 41.5-43°C. (Lit. 43°C.)

5-Dimethylamino-1,2,3,4-thiatriazole (IV) was prepared according to Lieber³⁶; m.p. 49-50°C. (Lit. 51°C.)

1,2,4-Triazoles

1,1-Dimethyl-3-methylaminoguanidinium iodide was prepared by a slight modification of a procedure developed by Finnegan et al.¹⁴⁰. 23.0 g (0.1 mol) of 1,1-dimethyl-3-aminoguanidinium iodide¹⁴¹ was suspended in ethanol and 9.5 ml of formaldehyde solution (35 % in water) was added. The mixture was shaken until solution occurred and then hydrogenated over 0.3 g of PtO_2 (Adam's catalyst) at room temperature and at an initial pressure of 50 p.s.i. After five hrs the theoretical amount of hydrogen had been taken up. Evaporation gave a solid residue (12.5 g, 51 %) which could be recrystallized from acetone-ether with cooling; m.p. 125.5-127°C. Calcd. for $C_4H_{13}IN_4$ (244.08): C 19.7; H 5.37; N 23.0; I 52.0. Found: C 19.7; H 5.44; N 23.6; I 51.7.

3-Dimethylamino-1-methyl-1,2,4-triazole (Va). A solution of 5 g (0.020 mol) of 1,1-dimethyl-3-methylaminoguanidinium iodide in 15 ml of formic acid was refluxed for 48 hrs. The mixture was then made alkaline with 2M NaOH and extracted with chloroform. Evaporation of the chloroform solution gave 1.9 g (76 %) of the crude product, which was distilled at 48-49°C (0.4 mm). Calcd. for $C_5H_{10}N_4$ (126.16): C 47.6; H 7.99; N 44.4. Found: C 47.6; H 8.35; N 44.0.

3-Nitrosomethylamino-1-methyl-1,2,4-triazole. 1.3 g (0.010 mol) of Va was dissolved in acetic acid (10 ml). 0.9 ml of fuming nitric acid in acetic anhydride (10 ml) was added dropwise. The reaction mixture was stirred for one hr and then poured onto ice. The resulting water solution was neutralized with NaOH and then extracted with chloroform. Evaporation of the chloroform layer yielded 0.9 g (64 %) of the nitroso compound; m.p. 88-89°C after recrystallization from toluene. The product gave a positive Liebermann nitroso test. NMR ($CDCl_3$): δ = 3.45 (3H; NMe(NO)); δ = 3.98 (3H; NCH_3) and δ = 8.13 (1H; CH). Calcd. for $C_4H_7N_5O$ (141.13): C 34.0; H 5.00; N 49.9. Found: C 34.0; H 5.04; N 49.7. The same product was obtained in 54 % yield when compound Va was mixed with fuming nitric acid and conc. sulphuric acid.

3-Dimethylamino-1,5-dimethyl-1,2,4-triazole (Vb). 4.4 g (0.050 mol) of 1-acetyl-1-methylhydrazine¹⁴² and 3.5 g (0.050 mol) of dimethylcyanamide, dissolved in conc. hydrochloric acid (5 ml), were heated on a water bath for 1.5 hr and then cooled. 25.5 ml of 2M NaOH was added and the reaction mixture was heated for another 40 min. Extraction with chloroform and evaporation of the chloroform solution gave an oily residue, which crystallized on cooling. The yield was 3.2 g (47 %), m.p. 70-71.5°C after recrystallization from ligroin. Calcd. for $C_6H_{12}N_4$ (140.19): C 51.4; H 8.63; N 40.0. Found: C 51.3; H 8.67; N 40.4.

3-Dimethylamino-2-methyl-1,2,4-triazole (Vc) was prepared according to Bagal et al.⁴¹ by heating 1-amino-1,2,2-trimethylguanidinium iodide with formic acid for 40 hrs at 110°C. B.p. 98-99°C (21 mm). The product was characterized as the picrate, m.p. 152-153.5°C. (Lit.⁴¹ 152-153°C.)

3-Dimethylamino-1-methyl-5-nitro-1,2,4-triazole (Vd) was obtained from 1-methyl-3,5-dinitro-1,2,4-triazole and dimethylamine according to Bagal *et al.*⁴¹, m.p. 108-109°C after recrystallization from ethanol. (Lit. m.p. 109°C.)

3-Dimethylamino-4-methyl-1,2,4-triazole (Ve). The hydro iodide,, prepared according to Kröger *et al.*⁴⁰, was treated with 2M NaOH to alkaline reaction. Extraction with chloroform and evaporation of the chloroform layer gave the desired product in almost quantitative yield; b.p. 128-129°C (0.8 mm). Calcd. for $C_8H_{10}N_4$ (126.16): C 47.6; H 7.99; N 44.4. Found: C 47.2; H 8.10; N 44.7.

Dimethylamino salt of 3,5-dinitro-1,2,4-triazole (Vg). 3.16 g (0.02 mol) of 3,5-dinitro-1,2,4-triazole⁴¹ was dissolved in dioxane (50 ml) and mixed with 4.5 g (0.04 mol) of dimethylamine solution (40 % in water). The mixture was heated in a sealed tube for one hr at 75-80°C. After cooling, 1.6 g (39 %) of the salt precipitated. Another 1.3 g (32 %) was obtained on removal of the solvent and treatment of the remaining crystalline mass with *iso*-propanol. Recrystallization from ethanol gave m.p. 185-186°C. Calcd. for $C_4H_8N_6O_4$ (204.15): C 23.5; H 3.95; N 41.2. Found: C 23.6; H 4.04; N 40.9. Heating Vg with dimethylamine in water at 200°C in a sealed tube for 24 hrs gave no further reaction.

Tetrazoles

5-Dimethylamino-2-methyl-tetrazole (VIa) and 5-dimethylamino-1-methyl-tetrazole (VIb). 5 g (0.044 mol) of 5-dimethylamino-tetrazole⁴³ was treated with diazomethane in ether at 0°C. The mixture was allowed to stand over night, slowly warming up to room temperature. The ether was removed and the residue was, according to NMR, an isomeric mixture of VIa and VIb. Distillation gave 2.1 g (38 %) of the 2-methyl compound at 40-42°C (0.4 mm), and 1.2 g (21 %) of the 1-methyl compound at 96-100°C (0.4 mm). The latter compound was in every respect identical with a sample of 5-dimethylamino-1-methyl-tetrazole prepared

unambiguously from 1-amino-2,3,3-trimethylguanidinium iodide and nitrous acid⁴⁴. Calcd. for the 2-methyl compound $C_4H_9N_5$ (127.15): C 37.8; H 7.13; N 55.1. Found: C 37.5; H 7.42; N 55.0.

REFERENCES

1. G. Binsch in "Topics in Stereochemistry", Vol. 3, E.L. Eliel and N.L. Allinger, Eds., Interscience Publishers, John Wiley, New York, 1968, p. 132.
2. H. Kessler, Angew. Chem. 82, 237 (1970).
3. R.K. MacKenzie and D.D. MacNicol, Chem. Comm. 1299 (1970).
4. A.R. Katritzky and G.J.T. Tiddy, Organic Magnetic Resonance 1, 57 (1969).
5. D.D. MacNicol, Chem. Comm. 933 (1969).
6. J. Almog, A.Y. Meyer and H. Shanan-Atidi, J. Chem. Soc. Perkin II 451 (1972).
7. R.R. Shoup, H.T. Miles and E.D. Becker, J. Phys. Chem. 76, 64 (1972).
8. D.M.G. Martin and C.B. Reese, Chem. Comm. 1275 (1967).
9. Z. Neiman and F. Bergmann, Chem. Comm. 1002 (1968).
10. M.J.S. Dewar, A.J. Harget and F.R.S. Harget, Proc. Roy. Soc. London A 315, 443 (1970)
11. I. Fischer-Hjalmars, Tetrahedron 19, 1805 (1963).
12. S. Forsén and P.N. Skancke in "Selected Topics in Structure Chemistry", Universitetsförlaget, Oslo, 1967, p. 229.
13. A. Skancke, Acta Chem. Scand. 24, 1389 (1970).
14. C.I. Ghirvu, O. Gropen and P.N. Skancke, Acta Chem. Scand. 25, 2023 (1971).
15. K.N. Shaw and L.W. Reeves, Chem. Phys. Letters 10, 89 (1971).
16. O. Gropen and H.M. Seip, Chem. Phys. Letters 11, 445 (1971).
17. I.D. Rae and L.K. Dyllal, Aust. J. Chem. 19, 835 (1966).
18. P. Grammaticakis, Bull. Soc. Chim. France 207 (1953).
19. P. Grammaticakis, Bull. Soc. Chim. France 220 (1951).
20. G. Pulvermacher, Chem. Ber. 27, 613 (1894).
21. M. Freund and C. Meinecke, Chem. Ber. 29, 2511 (1896).
22. R. Stolle and K. Fehrenbach, J. prakt. Chem. [2] 122, 298 (1929).
23. S. De, J. Indian Chem. Soc. 7, 651 (1930).

24. H. Gehlen and K. Möckel, *Ann. Chem.* 660, 144 (1962).
25. M.S. Gibson, *Tetrahedron* 18, 1377 (1962).
26. H. Najer, R. Giudicelli, C. Morel and J. Menin,
Bull. Soc. Chim. France 153 (1966).
27. G. Young and W. Eyre, *J. Chem. Soc.* 79, 54 (1901).
28. G. Werber and F. Maggio, *Ann. Chim. (Rome)* 49, 2124 (1959).
29. E. Hoggarth, *J. Chem. Soc.* 1163 (1949).
30. J. Goerdeler, J. Ohm and O. Tegtmeier, *Chem. Ber.* 89,
1534 (1956).
31. U.S. Patent 2,790,791 (1957); *Chem. Abstr.* 51, 13402 (1957).
32. J. Sandström in "Advances in Heterocyclic Chemistry", Vol.
9, A.R. Katritzky and A.J. Boulton, Eds., Academic Press,
New York, 1968, p. 198.
33. W. Lehnert, *Tetrahedron Letters* 1501 (1971).
34. J. Goerdeler and W. Roth, *Chem. Ber.* 96, 534 (1963).
35. J. Goerdeler, H. Groschopp and U. Sommerlad,
Chem. Ber. 90, 182 (1957).
36. E. Lieber, C.N.R. Rao, C.B. Lawryer and J.P. Trivedi,
Can. J. Chem. 41, 1643 (1963).
37. E. Åkerblom, *Acta Chem. Scand.* 19, 1142 (1965).
38. V.Ya. Grinsteins and G.I. Cipens, *J. Gen. Chem. USSR.*
31, 818 (1961).
39. G.I. Cipens and V.Ya. Grinsteins, *J. Gen. Chem. USSR.*
32, 3739 (1962).
40. C.-F. Kröger, G. Schoknecht and H. Beyer, *Chem. Ber.* 97,
396 (1964).
41. L.I. Bagal, M.S. Pevzner and V.Ya. Samarenko, *Khim.*
Geterotsikl. Soedin. 2, 269 (1970).
- 42a A.G. Burton, R.O. Frampton, C.D. Johnson and A.R. Katritzky,
J. Chem. Soc. Perkin II 1940 (1972).
- 42b J.E. Oliver and J.B. Stokes, *J. Heterocycl. Chem.* 7, 961
(1970).
43. K.A. Jensen, A. Holm and S. Rachlin, *Acta Chem. Scand.*
20, 2803 (1966).
44. D.B. Murphy and J.P. Picard, *J. Org. Chem.* 19, 1807 (1954).
45. F. Bloch, *Phys. Rev.* 70, 460 (1946).

46. H.S. Gutowsky, D.W. McCall and C.P. Slichter, J. Chem. Phys. 21, 279 (1953).
47. H.M. McConnell, J. Chem. Phys. 28, 430 (1958).
48. I.O. Sutherland in "Annual Reports on NMR Spectroscopy", Vol. 4, E.F. Mooney, Ed., Academic Press, London, 1971.
49. Copyright 1965, J.P. Chandler, Physics Department, Indiana University.
50. K.A. Jensen and J. Sandström, Acta Chem. Scand. 23, 1911 (1969). The formula in this reference is in error by a factor of 2.
51. S. Glasstone, K.J. Laidler and H. Eyring, "The Theory of Rate Processes", McGraw-Hill, New York, 1941, p. 190.
52. H.S. Gutowsky and C.H. Holm, J. Chem. Phys. 25, 1228 (1956).
53. H.J. Jakobsen and H. Lund. Personal communication.
54. W.G. Salmond, Quart. Rev. 22, 253 (1968).
55. H.H. Szmant and H.J. Planinsek, J. Am. Chem. Soc. 72, 4981 (1950).
56. M. Horak, I.J. Hymans and E.R. Lippincott, Spectrochim. Acta 22, 1355 (1966).
57. M.J.S. Dewar and E.A.C. Lucken, J. Chem. Soc. 426 (1959).
58. D.T. Clark, Tetrahedron 24, 2663 (1968).
59. D.T. Clark, Chem. Comm. 319 (1970).
60. H.H. Jaffé, Chem. Rev. 53, 191 (1953).
61. D.P. Craig, A. Maccoll, R.S. Nyholm, L.E. Orgel and L.E. Sutton, J. Chem. Soc. 332 (1954).
62. W. Moffitt, Proc. Roy. Soc. London A 200, 409 (1950).
63. P.T. Inglefield and S. Kaplan, Can. J. Chem. 50, 1594 (1972).
64. R.E. Klinck, D.H. Mair and J.B. Stothers, Chem. Comm. 409 (1967).
65. I. Wennerbeck and J. Sandström, Organic Magnetic Resonance, in press.
66. R. Pariser and R.G. Parr, J. Chem. Phys. 21, 466 (1953).
67. R. Pariser and R.G. Parr, J. Chem. Phys. 21, 767 (1953).
68. J.A. Pople, Trans. Faraday Soc. 49, 1375 (1953).
69. C.C.J. Roothaan, Rev. Mod. Phys. 23, 69 (1951).
70. R.G. Parr, J. Chem. Phys. 20, 239 (1952).

71. M. Goeppert-Mayer and A.L. Sklar, J. Chem. Phys. 6, 645 (1938).
72. I. Fischer-Hjalmars, J. Chem. Phys. 42, 1962 (1965).
73. J. Hinze and H.H. Jaffé, J. Am. Chem. Soc. 84, 540 (1962).
74. K. Nishimoto and N. Mataga, Z. Phys. Chem. 13, 140 (1957).
75. R. Pariser, J. Chem. Phys. 21, 568 (1953).
76. H. Kon, Bull. Chem. Soc. Japan 18, 275 (1955).
77. R. Phan-Tan-Luu, L. Bouscasse, E.J. Vincent and J. Metzger, Bull. Soc. Chim. France 3283 (1967).
78. M.J.S. Dewar and T. Morita, J. Am. Chem. Soc. 91, 796 (1969).
79. M.J.S. Dewar and N. Trinajstić, J. Am. Chem. Soc. 92, 1453 (1970).
80. B. Roos and P.N. Skancke, Acta Chem. Scand. 21, 233 (1965).
81. R.G. Parr, J. Chem. Phys. 20, 1499 (1952).
82. B. Roos, Acta Chem. Scand. 21, 2318 (1967).
83. O. Gropen and P.N. Skancke, Acta Chem. Scand. 24, 1768 (1970).
84. I. Fischer-Hjalmars and M. Sundbom, Acta Chem. Scand. 22, 607 (1968).
85. A. Skancke and P.N. Skancke, Acta Chem. Scand. 24, 23 (1970).
86. H. Jensen and P.N. Skancke, Acta Chem. Scand. 22, 2899 (1968).
87. G. Höjer, Acta Chem. Scand. 23, 2589 (1969).
88. O. Gropen and P.N. Skancke, Acta Chem. Scand. 23, 2685 (1969).
89. J.A. Pople and G.A. Segal, J. Chem. Phys. 44, 3289 (1966).
90. D.P. Santry and G.A. Segal, J. Chem. Phys. 47, 158 (1967).
91. J.A. Pople and D.L. Beveridge, "Approximate Molecular Orbital Theory", McGraw-Hill, New York, 1970.
92. B. Bak, L. Nygaard, E.J. Pedersen and J. Rastrup-Andersen, J. Mol. Spectroscopy 19, 283 (1966).
93. L. Nygaard, R.L. Hansen, J.T. Nielsen, J. Rastrup-Andersen, G.O. Sörensen and P.A. Steiner, J. Mol. Structure 12, 59 (1972).
94. S.V. Dobyons and L. Pierce, J. Am. Chem. Soc. 85, 3553 (1963).
95. M. Roche, Ph.D. Thesis, The University of Aix-Marseille, France, 1970.
96. "Tables of Interatomic Distances and Configuration in Molecules and Ions". Special publ. no. 11. The Chemical Society, London, 1958.

97. M.J.S. Dewar, F.R.S. Harget and A.J. Harget, Proc. Roy. Soc. London A 315, 457 (1970).
98. B. Nelander, Theor. Chim. Acta 25, 382 (1972).
99. R.K. Harris and R.A. Spragg, Chem. Comm. 362 (1967).
100. W.G. Fateley, R.K. Harris, F.A. Miller and R.E. Witkowsky, Spectrochim. Acta 21, 231 (1965).
101. T. Drakenberg and J.M. Lehn, J. Chem. Soc. Perkin II 532 (1972).
102. M.J.S. Dewar, "The Molecular Orbital Theory of Organic Chemistry", McGraw-Hill, New York, 1969, p. 376.
103. J. Sandström, J. Phys. Chem. 71, 2318 (1963).
104. G. Robinet, F. Crasnier, J.-F. Labarre and C. Leibovici, Theor. Chim. Acta 25, 259 (1972).
105. S. Ljunggren and G. Wettermark, Theor. Chim. Acta 19, 326 (1970).
106. R.T.C. Brownlee and R.W. Taft, J. Am. Chem. Soc. 92, 7007 (1970).
107. R.T.C. Brownlee and R.W. Taft, J. Am. Chem. Soc. 90, 6537 (1968).
108. R.M. Stevens, J. Chem. Phys. 52, 1397 (1970).
109. D.G. Lister and J.K. Tyler, Chem. Comm. 152 (1966).
110. J.C.D. Brand, D.R. Williams and T.J. Cook, J. Mol. Spectroscopy 20, 359 (1966).
111. W.J. Hehre, L. Radom and J.A. Pople, J. Am. Chem. Soc. 94, 1496 (1972).
112. L. Radom, W.J. Hehre and J.A. Pople, J. Am. Chem. Soc. 94, 2371 (1972).
113. H.A. Scheraga in "Advances in Physical Organic Chemistry", Vol. 6, Academic Press, New York, 1968, p. 103.
114. M.J.S. Dewar and M.C. Kohn, J. Am. Chem. Soc. 94, 2699 (1972).
115. H.-J. Köhler and F. Birnstock, Z. Chem. 12, 196 (1972).
116. J.A. Pople, W.G. Schneider and H.J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, 1959, p. 74.
117. W. McFarlane, J. Chem. Soc. (B) 28 (1969).

118. J.A. Pople, W.G. Schneider and H.J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, 1959, chapter 7.
119. J.A. Pople, Discuss. Faraday Soc. 34, 7 (1962).
120. P. Lazzaretti and F. Taddei, Tetrahedron Letters 3025 (1969).
121. T.B. Cobb and J.D. Memory, J. Chem. Phys. 50, 4262 (1969).
122. G. Leandri, A. Mangini, F. Montanari and R. Passerini, Gazz. Chim. Ital. 85, 769 (1955).
123. M.R. Padhye and J.C. Patel, J. Sci. Ind. Res. (India) B15, 49 (1956).
124. W.F. Forbes, W.A. Mueller, A.S. Ralph and J.F. Templeton, Can. J. Chem. 35, 1049 (1957).
125. E. Merkel, Z. Elektrochem. 63, 373 (1959).
126. W.M. Schubert and J. Robins, J. Am. Chem. Soc. 80, 559 (1958).
127. H.H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy", John Wiley, New York, 1962, p. 410-412.
128. E. Lieber, J. Ramachandran, C.N.R. Rao and C.N. Pillai, Can. J. Chem. 37, 563 (1959).
129. C. Ainsworth, J. Am. Chem. Soc. 87, 5800 (1965).
130. A. Burawoy and J.P. Critchley, Tetrahedron 5, 340 (1959).
131. B.F. Day, T.W. Campbell and G.M. Coppinger, J. Am. Chem. Soc. 73, 4687 (1951).
132. E. Testa, G.G. Gallo, F. Fava and G. Weber, Gazz. Chim. Ital. 88, 812 (1958).
133. J.N. Murrell, "The Theory of the Electronic Spectra of Organic Molecules", Methuen & Co Ltd., London, 1963, p.195.
134. M.R. Atkinson, E.A. Parkers and J.B. Polya, J. Chem. Soc. 4256 (1954).
135. B. Elpern and F.C. Nachod, J. Am. Chem. Soc. 72, 3379 (1950).
136. C. Vogelesang, Rec. Trav. Chim. 62, 10 (1943).
137. K.A. Jensen, J. prakt. Chem. 159, 189 (1941).
138. I. Lalezari and N. Shargi, J. Heterocycl. Chem. 3, 336 (1971).

139. K.A. Jensen, U. Anthoni, B. Kägi, C. Larsen and C.Th. Pedersen, *Acta Chem. Scand.* 22, 47 (1968).
140. W.G. Finnegan, R.A. Henry and G.B.L. Smith, *J. Am. Chem. Soc.* 74, 2981 (1952).
141. K.A. Jensen and C.Th. Pedersen, *Acta Chem. Scand.* 15, 1000 (1961).
142. C.Th. Pedersen, *Acta Chem. Scand.* 18, 2199 (1964).

